University of Alberta

Physical activity as a supportive care intervention in palliative cancer patients

by

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Abstract

Objective: To explore the role of physical activity as a supportive care intervention in palliative cancer patients.

Methods: Study one is a systematic review of physical activity as a supportive care intervention in palliative cancer patients. Study two is a cross-sectional survey examining the physical activity preferences, interests and quality of life associations of palliative cancer patients. Study three is a case series examining a home-based physical activity program in palliative cancer patients.

Results: A majority of palliative cancer patients expressed interest in participating in a physical activity program. Greater levels of physical activity were associated with higher quality of life scores. Select palliative cancer patients were able to complete a home-based physical activity program.

Conclusions: There is a potential role for physical activity as a positive supportive care intervention in palliative cancer patients. Overall findings point towards a future feasibility trial.

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LIST OF ABBREVIATIONS

1-RM	1-repetition maximum
ANCOVA	Analysis of covariance
ANOVA	Analysis of variance
BFI	Brief Fatigue Inventory
bpm	Beats per minute
CAGE	Screen for alcohol abuse
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
CRF	Cancer-related fatigue
d	Cohen's effect size
EORTC QLQ-C30	European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire
ESAS	Edmonton Symptom Assessment Scale
FACIT-F	Functional Assessment of Chronic Illness Therapy – Fatigue Version IV
FEV_1	Forced expiratory volume in 1 second
FQ	Fatigue Questionnaire
FVC	Forced vital capacity
GIQLI	Gastrointestinal Quality of Life Index
GLTEQ	Godin Leisure-Time Exercise Questionnaire
HADS	Hospital Anxiety and Depression Scale
HDS	Hope Differential – Short Instrument

KPS	Karnofsky Performance Score
KSC	Kerry S. Courneya
LLFDI	Late-Life Function and Disability Instrument
MFI	Multidimensional Fatigue Inventory
MID	Minimal important difference
MQOL	McGill Quality of Life Questionnaire
NK	Natural killer cell
PACC	Physical Activity and Cancer Control
PASE	Physical Activity Scale for the Elderly
PPS	Palliative Performance Scale
QoL	Quality of life
RCT	Randomized controlled trial
SD	Standard deviation
SDS	Symptom Distress Scale
SF-36	Short Form 36 Survey
SFT	Seniors Fitness Test
SIGLE	System for Information on Grey Literature
SMW	Sharon M. Watanabe
SPSS	Statistical Package for the Social Sciences
SSL	Sonya S. Lowe

UE/LE	Upper extremity / Lower extremity
VC	Vital capacity
VO_2max	Peak oxygen uptake
WBRT	Whole brain radiotherapy
WHO	World Health Organization

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I: CHAPTER ONE

INTRODUCTION

I-1. OVERVIEW OF THE THESIS

Increasing attention has been given to physical activity as an intervention to improve supportive care outcomes in cancer patients. Recent meta-analyses have reported that physical activity can positively benefit several aspects of physical and psychological well-being that contribute to quality of life in early stage cancer patients (1). The difference in disease and symptom burden between early-stage cancer patients and those with progressive, metastatic, incurable cancer, renders it difficult to generalize these benefits across the cancer spectrum. Currently, there exists a critical gap in our knowledge of the potential benefits of physical activity in the palliation stage of cancer control (2). The purpose of this thesis was to examine the role of physical activity as a supportive care intervention in palliative cancer patients. A secondary objective of this thesis was to examine the feasibility of a physical activity intervention in a palliative cancer population.

The first section of this introduction provides an overview of cancer and palliative care, with emphasis on the physical challenges facing patients at the palliative period of the cancer spectrum. The concluding section of this introduction provides an overview of physical activity as supportive therapy in cancer patients. The main body of the thesis consists of three chapters. Chapter Two is a systematic review examining the best available evidence on physical activity as a supportive care intervention in palliative cancer patients. Chapter Three presents the findings of a pilot survey examining the physical activity preferences, interests and quality of life associations of palliative cancer patients. Based on the findings of this pilot survey,

Chapter Four presents a case series examining the initial development and feasibility testing of a home-based physical activity program in palliative cancer patients. Finally, the overall conclusions, practical implications and future research directions of this work are discussed.

I-2. STATEMENT OF THE PROBLEM

Cancer is one of the leading causes of mortality and morbidity worldwide (2). The resultant morbidities of cancer and its treatment are manifold; common physical symptoms include pain, muscle weakness and fatigue, whereas common psychological symptoms include depression, anxiety and poor sense of well-being. The impact of these distressing symptoms increases with disease burden, particularly at the end stages of cancer. In the palliative care of cancer patients, alleviating suffering and maximizing quality of life becomes the primary goal (3).

Physical activity has been shown to improve several aspects of physical and psychological well-being that contribute to quality of life in early stage cancer patients (4), but few studies have focused on cancer patients at the palliative phase of the cancer spectrum. As identified by the *Physical Activity and Cancer Control* (PACC) framework, there is increasing evidence that physical activity can positively affect supportive care outcomes in many cancer control categories, however "research on physical activity and cancer palliation is still very limited" (5). Given that this palliative phase is when a cancer patient's quality of life could potentially benefit the most, there exists a critical need to investigate physical activity as a supportive care intervention in this population.

Within this thesis, the role of physical activity as a supportive care intervention in palliative cancer patients was explored in an attempt to characterize their physical activity interests and preferences, and to examine the feasibility of a physical activity intervention in this population.

I-3. REVIEW OF CANCER AND PALLIATIVE CARE

The leading life-threatening illness worldwide is cancer (2). Cancer is estimated to account for 7.6 million deaths, approximately one in eight deaths worldwide (6). In 2007, cancer will cause an estimated 72,700 deaths in Canada alone (7). Approximately 159,900 new cases of cancer will be diagnosed in Canada this year, with rising incidence due to an increase in the aging population. As methods of cancer detection and treatment improve, survival is prolonged and the lifetime burden of distressing physical and psychosocial symptoms increases. Addressing these issues is critical towards maximizing quality of life, a multidimensional construct encompassing all physical and psychosocial factors (8).

Improving quality of life is the primary goal of palliative care (9). According to the World Health Organization (WHO), palliative care is the multidisciplinary and holistic assessment and management of physical, psychosocial and spiritual symptoms, with the goal of alleviating suffering (10). This definition can encompass a wide chronological range within the spectrum of cancer control, from those who are newly diagnosed with life-threatening illness (e.g., stage IV lung cancer), to those who are undergoing chemotherapy and radiotherapy for symptom management (e.g., breast cancer with bone metastases), and those who are eligible for hospice care or

who are actively dying. Thus the mandate of palliative care can apply throughout the cancer trajectory, with its greatest impact being at the end stages of life (11).

Given these broadly inclusive aims, the lack of uniform criteria for defining palliative care populations is a well-recognized limitation in oncologic research (12); there is no consensus as to what time-point in life expectancy can the cancer patient be considered "palliative" or "terminal" (13). Despite these challenges, it is recognized that the closer the patient is towards death, the greater the disease and symptom burden becomes thus making palliation the sole focus of care (14). The U.S. National Cancer Institute defines advanced cancer as "cancer that has spread to other places in the body and usually cannot be cured or controlled with treatment" (15). For the purposes of this thesis, the palliative cancer patient will be defined as a patient who has progressive, incurable, and locally recurrent or metastatic cancer, with a survival of less than 12 months. Alleviating symptom burden despite incurable disease is therefore key towards improving quality of life in palliative cancer patients.

I-4. REVIEW OF CANCER-RELATED FATIGUE IN PALLIATIVE ONCOLOGY

The most common symptom reported by palliative cancer patients is cancer-related fatigue (CRF) (16). Between 60-90% of advanced cancer patients report experiencing CRF, and rate CRF as the symptom with the most negative impact on overall quality of life (17). CRF is a multidimensional phenomenon comprised of physical and psychological symptoms which cause significant distress: exhaustion, diminished physical capacity, lack of motivation and impaired mental functioning

(18). Given its profound impairment of quality of life, CRF has been identified as a key priority in palliative care research (16).

Given the high tumor and symptom burden in palliative cancer patients, there may be multiple interrelated etiologies for CRF in this population (19). Physiologically, tumor load and subsequent pro-inflammatory cytokine production, such as interleukin-1, interleukin-6 and tumor necrosis factor-α, interact to contribute to CRF in the end stages of cancer. In combination with progressive metabolic abnormalities and autonomic failure, these cytokines are key mediators of anemia, anorexia-cachexia and fever, all of which contribute to CRF. Psychologically, the high prevalence of depression and anxiety in palliative cancer patients may compound the cognitive and affective difficulties as a result of CRF. The increasing use of medications, such as opioid analgesics and anxiolytics, to palliate these individual symptoms may likewise worsen CRF.

One of the devastating repercussions of CRF is loss of physical function, which has been reported by palliative cancer patients as one of their primary concerns at the end of life (20). Neurohormonal abnormalities and anorexia-cachexia result in extensive loss of skeletal muscle mass in the advanced cancer patient. Progressive deconditioning and impaired mobility lead to a loss of independence in activities of daily living; this decline in physical function thus compounds the fear of becoming a burden to others, which can trigger severe emotional distress in the advanced cancer patient (21). Optimizing physical function with the aim of maintaining autonomy is therefore critical in maximizing overall quality of life in palliative cancer patients.

I-5. REVIEW OF EXERCISE ONCOLOGY

Given the impact of CRF and subsequent functional impairments on quality of life in cancer patients, recent attention has been given to physical activity as an intervention to improve these outcomes. Physical activity is defined as any bodily movement produced by the skeletal muscles that results in a substantial increase in energy expenditure over resting levels; exercise is any form of physical activity which an individual undertakes during leisure time and that is done repeatedly over an extended time period with the goal of improving fitness or health (22). Increasing evidence indicates a role for physical activity in improving several aspects of physical and psychological well-being that may contribute to quality of life in cancer patients, including muscle strength, functional capacity, mood and self-esteem (4).

Recent systematic reviews have indicated trends towards positive effects of physical activity interventions on cancer patients on a variety of outcomes. Knols et al. (2005) evaluated 34 randomized controlled and controlled clinical trials examining the effectiveness of physical exercise in cancer patients during and after medical treatment (23). The selected trials examined exercise during and after treatment of breast cancer, mixed solid tumor, bone marrow and peripheral stem cell transplantation groups. There were no identified studies examining palliative patients. Overall, the authors concluded that benefits from physical activity have been observed for quality of life, objective functioning and self-report symptom measures, particularly CRF, in cancer patients; these positive effects, however, "may vary significantly as a function of the type of cancer and the stage of disease" (23). Given

the variability in both disease and symptom burden at the end stages of cancer, these conclusions have limited applicability to palliative cancer populations.

Conn et al. (2006) conducted a meta-analysis of 30 randomized, non-randomized controlled and uncontrolled trials which tested exercise interventions among adult cancer patients, using weighted mean effect sizes (1). The majority of selected studies assessed supervised exercise interventions in breast cancer patients, and subsequent overall effects were stratified according to single-group versus two-group comparisons. The authors determined that exercise interventions in cancer patients produced modest overall effect sizes for most outcomes, including quality of life, physical function and CRF; these conclusions, however, can "only be generalized to members of the populations sampled in these studies" (1). This limitation is particularly relevant given that no studies involving palliative cancer populations were included.

Schmitz et al. (2005) performed a systematic qualitative and quantitative review of 32 randomized controlled and controlled clinical trials determining the effectiveness of physical activity interventions, alone or combined with dietary co-interventions, in improving outcomes in cancer patients (24). 63% of included trials examined exercise interventions during active cancer treatment, and over 70% were conducted in breast cancer patients. There were no identified studies focused on palliation. Overall, there was weak qualitative evidence for consistent positive effect of physical activity interventions on quality of life during cancer treatment, and quantitative analysis yielded null findings for the effect of physical activity on CRF during and after treatment. Given that differences in disease stage could alter the

effectiveness of physical activity interventions, the authors highlighted the lack of syntheses of physical activity studies on specific cancer control outcomes, such as "palliation of symptoms at the end of life" (24).

In summary, there is preliminary evidence that physical activity interventions can impact positively on supportive care outcome measures in cancer patients both during and after treatment. However, each of these reviews have consistently noted that these findings could not be generalized to those at the end stages of cancer. Given the significance of maximizing quality of life, there exists a critical gap in the literature with regards to physical activity as a supportive care intervention in palliative cancer patients.

I-6. STUDY PURPOSES

The primary purposes of this thesis were to: (a) conduct a qualitative systematic review of the best available evidence on physical activity as a supportive care intervention in palliative cancer patients, (b) explore the physical activity preferences, interests and quality of life associations of palliative cancer patients, and (c) examine the initial development and feasibility testing of a home-based physical activity program in palliative cancer patients.

I-7. STUDY HYPOTHESES

I-7.1. For the systematic review, it was hypothesized that:

1. The best available evidence of physical activity as a supportive care intervention in palliative cancer patients would be low in quantity and quality.

2. Broadening the inclusion criteria for study design would yield the best available evidence of physical activity as a supportive care intervention in palliative cancer patients.

I-7.2. For the pilot survey, it was hypothesized that:

1. Few palliative cancer patients would be participating in any regular physical activity.
2. Palliative cancer patients that are participating in regular physical activity would report better physical functioning, less severe symptoms, and better quality of life.
3. A majority of the palliative cancer patient population would be interested and feel able to participate in a physical activity intervention.

I-7.3. For the case series, it was hypothesized that:

1. An individualized home-based physical activity program would be feasible in terms of adherence and tolerability for palliative cancer patients.
2. Palliative cancer patients who completed an individualized home-based physical activity program would show improvement in patient-reported physical function and quality of life outcomes.

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II. CHAPTER TWO

"Physical Activity as a Supportive Care Intervention in Palliative Cancer Patients: A Systematic Review"

II-1. INTRODUCTION

Palliative care is the interdisciplinary and holistic management of progressive, advanced disease, wherein prognosis is limited and the primary goal is quality of life (QoL) (1). In the end stages of illness, overall QoL can encompass physical, psychosocial and spiritual issues for both the patient and their family. The progression of disease is often accompanied by the escalation of symptoms, such as pain and fatigue, which can contribute greatly to total suffering. Alleviating suffering is a key aim of palliation, and minimizing symptomatic burden can apply throughout the illness trajectory, particularly at the end stages of disease (2).

Palliative care is a key component of the management of cancer. In Canada alone, an estimated 159,900 new cancer diagnoses and 72,700 deaths from cancer will occur in 2007 (3). The Canadian Hospice Palliative Care Association estimates that over 65% of annual deaths in Canada will require access to hospice palliative care services (4). As both screening and treatment modalities for cancer improve, patients are living longer with cancer and its associated symptoms; disease and symptom burden are particularly compounded in palliative cancer patients. Thus the role of palliative care in targeting symptoms, and thereby improving overall QoL in advanced cancer patients, becomes more crucial.

Among the most devastating and disruptive symptoms of cancer are cancer-related fatigue (CRF) and loss of physical function (5). CRF is defined as a constant, subjective sensation of exhaustion, associated with cancer or its treatment, that impedes normal functioning and that is out of proportion to recent activity; the

prevalence of CRF amongst cancer patients is estimated between 60% and 90% (6). Loss of physical function can be attributed to CRF, as well as generalized muscle weakness and wasting due to anorexia-cachexia syndrome; this decline in physical function, and subsequent loss of mobility and independence, has been identified as one of the top distressing symptoms which negatively impact QoL in palliative cancer patients (7). The need for interventions targeting CRF and loss of physical function, therefore, is critical in cancer patients.

Physical activity is one potential intervention that can address this need in palliative cancer patients. Physical activity is defined as any bodily movement produced by the skeletal muscles that results in a substantial increase in energy expenditure over resting levels (8). In early stage cancer survivors, recent meta-analyses have shown that physical activity can positively affect a wide variety of outcomes, including cardiorespiratory fitness, mood, CRF, physical function and overall QoL (9). Disease and symptom burden, however, varies significantly across the cancer trajectory; given that CRF and loss of physical function become more disabling as cancer progresses, it is unclear if the benefits of physical activity generalize from early stage cancer patients to those with progressive, incurable disease.

A recent review of CRF and palliative care highlighted the need to delineate the types of physical activity interventions that would be most beneficial for end stage cancer patients to improve QoL outcomes (10). Although there are multiple prior reviews examining physical activity interventions in cancer patients, none have focused on palliative patients. To date, there is no rigorous systematic review of

physical activity interventions in palliative cancer patients. Here, we present the first systematic qualitative review of the best available evidence of physical activity as a supportive care intervention in palliative cancer patients.

II-2. METHODS

A search was conducted on the following electronic databases to March 2007: The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, CINAHL, PASCAL, SCOPUS, Web of Science, OCLC PapersFirst, OCLC ProceedingsFirst, Proquest Dissertations & Theses, PEDro, CIRRIE, RehabData and PubMED. The set of search terms for the MEDLINE database included the following: [(neoplasm$ or cancer$ or tumor$ or tumour$ or carcino$)] AND [(terminal care or terminally ill or terminal illness or terminal disease$ or palliat$ or hospice$ or terminal patient$) OR (end of life or survival time$ or life expectanc$ or near death or end stage$)] OR [(advanced adj3 cancer$) or (advanced adj3 neoplas$) or (metast$ or terminal cancer$)] AND [(dance therap$ or exercise$) or (exercise/ or exercise therapy/ or muscle stretching exercises/ or tai ji/ or walking/ or yoga) or (motion therap$ or physiother$ or physical therap$) or (dancing/ or bicycling/ or walking/ or weight lifting) or (physical activit$ or pilates$) or swimming]. This search strategy was modified as necessary for each database. The following journals were handsearched: Journal of Pain and Symptom Management (1998-present), Palliative Medicine (1998-present) and Supportive Care in Cancer (1997-present). The past 5 years of the following conference proceedings were handsearched: European Association of Palliative Care Congress and the Multinational Association of Supportive Care in Cancer International Symposium. In addition, reference lists of

all included studies were handsearched for additional studies. Where possible, study authors were contacted via email to identify unpublished studies and further relevant articles. Translation was conducted as required for non-English language articles.

II-2.1. Inclusion criteria

To be included in this review, a study had to examine a physical activity intervention in palliative cancer patients, aged 18 years or older, regardless of gender, tumor type or type of cancer treatment. For the purposes of this review, physical activity was defined as any bodily movement produced by the skeletal muscles that results in a substantial increase in energy expenditure over resting levels; exercise was defined as any form of physical activity which an individual undertakes during leisure time and that is done repeatedly over an extended time period with the goal of improving fitness or health (8). Palliative cancer was defined as progressive, incurable and locally recurrent or metastatic cancer, with a survival of less than 12 months. Randomized, non-randomized controlled and uncontrolled trials were included. Studies were required to have at least one of the following primary outcomes: patient-reported QoL, patient-reported physical functioning or patient-reported fatigue. Secondary outcomes of interest included objective measures of physical fitness, objective measures of physical functioning, and patient-reported symptoms. A decision was made *a priori* to exclude studies that involved a mixed population of different stages of disease, including palliative cancer patients, if they did not report data or analyze data separately for palliative patients. Data was extracted on the frequency, intensity and duration of physical activity, as well as recruitment, retention and adherence rates.

II-2.2. Study selection, data abstraction and quality assessment

Two independent reviewers (SSL, SMW) screened the titles and abstracts of the initial search of all databases to identify potentially relevant studies, and excluded those that were clearly irrelevant. All potentially relevant studies were obtained, and the same two independent reviewers (SSL, SMW) reviewed full papers against the inclusion/exclusion criteria. Data extraction on participants, methods, interventions, outcomes and adverse events was performed by the same 2 independent reviewers (SSL, SMW) onto forms designed and pilot-tested for this review. Disagreement regarding inclusion of studies was resolved by consensus, with arbitration by a third reviewer (KSC) if required. The same 2 independent reviewers (SSL, SMW) assessed the methodologic quality of each study using the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies 2003 (Thomas tool), rating each of the following study components as strong, moderate or weak: selection bias, study design, confounders, blinding, data collection methods and withdrawals/dropouts (11). The Thomas tool is rated as one of the six best tools for assessing quality of non-randomized studies in systematic reviews (12), and its individual component ratings are used to compare quality across studies.

Upon inspection of eligible studies, there was a high degree of clinical heterogeneity in terms of participants, interventions and outcomes, such that data pooling and quantitative analysis would not be appropriate. Data was therefore reviewed qualitatively for each included study, presenting effect estimates and statistical significance as reported in the original articles.

II-3. RESULTS

II-3.1. Search and Selection of Studies

The initial screen from all electronic databases identified 6036 studies, of which 154 were considered potentially relevant (see Figure II-1). Handsearching of journals and conference proceedings yielded 7 potentially relevant studies. 85 duplicates and 22 reviews were excluded, leaving a total of 47 potentially relevant papers (13-60). Study author contact yielded 1 potentially relevant unpublished study protocol (61). Non-English language articles were obtained and translated.

16 studies were excluded because they did not meet inclusion criteria for type of participant (13-16, 19, 22, 23, 28, 35, 41-43, 47, 52, 54, 58), and 20 studies were excluded because they did not meet inclusion criteria for type of intervention (17, 18, 20, 21, 24, 25, 29, 31, 33, 36-39, 44-46, 51, 53, 55, 60). 3 studies were excluded because of inadequate description of either the population or the intervention administered (30, 56, 61), and 2 studies did not report primary outcomes of interest for the review (40, 57). After a full text review, 6 studies were judged to meet the inclusion criteria (26, 27, 32, 34, 49, 50).

II-3.2. Overview of Included Studies

The 6 included studies involved a total of 84 participants in 5 countries (Australia, Austria, Germany, Norway and USA), published over a 6-year period (2000-2006) (see Table II-1). Of the 6 included studies, 3 were case reports, 2 were single group pre- to post-intervention trials, and 1 was a randomized controlled trial. All 6 studies were English language articles published in peer-reviewed journals. One of the included studies was described in two separate published articles (48, 49),

therefore data extraction was performed on both articles to obtain complete information for the single study.

3/6 of the included studies examined aerobic exercise interventions, whereas the other half examined mixed interventions involving both aerobic and resistance training components (see Table II-1). 4/6 studies involved hospital-based exercise training programs, with the remaining 2/6 studies examined home-based physical activity interventions. Of the 3 included studies with more than one participant, 1 study examined a group exercise intervention. The frequency of interventions ranged from biweekly to daily physical activity sessions, with the duration of intervention programs ranging from 4 to 52 weeks in length.

Two of the included case reports were published by Crevenna et al. (2003, 2003), who examined supervised ergometer bicycling interventions in two patients: (a) a 6-week program in a 55 year old male with metastatic hepatocellular carcinoma to the lung and brain (26), and (b) a 52-week program in a 48 year old female with metastatic breast cancer to the liver, lung and bone (27). The former participant was undergoing concurrent thalidomide treatment, and participated in twice weekly sessions with increasing workload to maintain heart rate at 60% of maximum workload for 60 minute sessions. The latter participant was undergoing concurrent palliative chemotherapy and radiotherapy, and participated in 60 minute sessions three times per week while systematically increasing workload according to the same criteria.

The third case report was published by Kelm et al. (2003), who examined a 13 week whole body strength and endurance training program in a 58 year old male

with rectal adenocarcinoma metastatic to the liver undergoing concurrent intrathecal chemotherapy (34). The participant completed biweekly sessions involving both strength training machines at 40%-60% of 1-repetition maximum, and treadmill walking or ergometer cycling with resistance and speed controlled to maintain a heart rate of between 130 to 150 beats per minute.

One of the uncontrolled trials was conducted by Porock et al. (2000), who examined an unsupervised home-based physical activity program in home hospice care patients in Australia (50). Their study sample was composed of 6 females and 3 males, with a mean age of 60 ± 10 years. The most common cancer diagnosis was bowel cancer, with 7 participants having metastases. Two participants reported undergoing concurrent chemotherapy, whereas 1 participant reported undergoing concurrent radiotherapy. The 4-week intervention consisted of an individualized home-based physical activity program, wherein participants could choose amongst a range of physical activities throughout the day; frequency and duration of each session was determined by how much activity the participant could tolerate, beginning with half that much several times daily (Winningham's half rule of thumb) (62). No method of progression of intervention workload was reported.

The second uncontrolled trial was published by Oldervoll et al. (2005, 2006), who examined a 6-week supervised group exercise program in outpatient clinic and hospice cancer patients with a clinician-estimated life expectancy between 3 and 12 months (49). Actual survival from time of study enrollment to time of death was not reported. The mean age of their study sample was 65±12 years, and the mean baseline Karnofsky Performance Score (63) was 83±13. The most common diagnosis was

gastrointestinal cancer (n=16), with 79% of participants reporting metastases. 26% of participants were undergoing concurrent chemotherapy, and 9% of participants were undergoing concurrent hormone therapy during the intervention period. Groups of between 3 to 8 participants performed a series of personalized circuit training stations focused on whole body muscle strength, standing balance and aerobic endurance for 50 minute sessions twice per week. No method of progression of intervention workload was reported.

The only randomized controlled trial (RCT) was published by Headley et al. (2004), who conducted an unsupervised, home-based seated exercise program in stage IV breast cancer patients receiving chemotherapy (32). Their study sample was composed of 38 females, with a mean age of 51±9 years. The participants performed a 30-minute seated exercise program using the Armchair Fitness: Gentle Exercise video in their own homes three times per week for a total of 12 weeks. Self-reported intensity was assessed using Borg Ratings of Perceived Exertion (64), however, no method of progression of intervention workload was reported.

Of the 3 included studies that had more than one participant, Headley et al.'s study (2004) did not report recruitment rates (32). Porock et al. (2000) reported that 46% (11/24) of approached patients agreed to participate (50), whereas Oldervoll et al. (2005) reported a 62% (63/101) recruitment rate (48). Four of the 6 studies did not report adherence rates; Crevenna et al. (2003) reported 100% adherence from its single participant with metastatic hepatocellular carcinoma (26), and Oldervoll et al. (2006) reported that an average of 10.6 out of 12 (88%) prescribed sessions were completed (49). Of the 3 included studies that had more than one participant, two

studies did not report retention rates; Oldervoll et al. (2006) reported that 34/47 (72%) participants completed the exercise intervention with all 34 participants (100%) completing follow-up assessments (48, 49).

In summary, there is significant clinical heterogeneity in terms of study designs, participants and interventions among the 6 included studies (see Table II-1). There is incomplete reporting of recruitment, adherence and retention rates. There is a wide variety of cancer diagnoses with differences in presence of metastases and concurrent therapy. There is variable reporting of specifics of the physical activity interventions administered, including frequency, intensity and duration. Due to this widespread diversity, quantitative comparisons between the included studies are not possible and thus only qualitative assessment is appropriate.

II-3.3. Methodological Quality of Included Studies

As assessed by the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies 2003 (Thomas Tool) (11), the overall methodologic quality of all 6 included studies was poor (see Table II-2). There is no evidence to support the summation of the Thomas Tool category scores as a means of comparing inter-study quality (65), therefore the individual component ratings are described qualitatively and compared across the included studies.

Five out of 6 studies were rated weak in the category of selection bias, which refers to the systematic differences in characteristics between the study sample and the target population for whom the intervention is intended. Of the studies with more than one participant, consecutive sampling was the most common method; subsequent findings from these study samples, therefore, are not generalizable to the

palliative cancer population as a whole. Volunteer bias is particularly relevant within the included case reports, as participants who volunteer may be healthier and have better baseline functional status than those who do not volunteer.

Five out of 6 studies were rated weak in the component of allocation bias, which is defined as the systematic differences in characteristics between groups given the method of assignment of participants to groups. The strength of study design lies in the presence of a comparison group, yet only one of the 6 studies had a control group. Despite using computer-based randomization of participants, however, Headley et al. (2004) did not report on allocation concealment and therefore the potential for bias still exists (32).

The third category of the Thomas Tool assesses confounders, which are characteristics that differ between groups and that are risk factors for intervention effects on the outcomes of interest (11). Baseline functional status and physical activity levels are among many factors which may significantly impact the effects of physical activity interventions (66). In Oldervoll et al.'s uncontrolled trial (2006), participants were recruited from both outpatient clinic and hospice sites; although hospice participants had a statistically significant lower baseline Karnofsky performance scores than outpatient participants ($p=0.003$), this was not accounted for in subsequent data analysis (49). Similarly, in Headley et al.'s RCT (2004), the control group had more participants with higher baseline physical activity levels, which was not adjusted for in their analysis (32).

None of the 6 included studies reported blinding, which the Thomas tool defines as the lack of knowledge of the participant's allocation such that the outcome

assessor is not influenced by detection bias (11). This is not to be unexpected given the nature of the interventions examined. Conversely, all 6 included studies were rated strong on the data collection component of the Thomas Tool. Each of the outcome measures used in all 6 included studies have been shown to be valid and reliable in cancer patients, although none of these tools were standardized across all studies.

Four out of 6 studies were rated strong for description of withdrawals and dropouts; however, these included the three case reports. The only included RCT failed to report any information about withdrawals or dropouts, and did not report using intention-to-treat analysis (32). Oldervoll et al.'s study (2006) showed significant withdrawal rates secondary to medical reasons (48), which reflects the significant loss to follow-up of larger palliative care trials (67). Without full disclosure of the outcomes of all participants, whether good or bad, the subsequent interpretation of findings may be flawed. With respect to analysis, only 2/6 studies were able to conduct inferential statistics on their data (32, 49).

Incomplete data reporting can influence intervention integrity, which assesses both the consistency of the intervention administered and the potential for contamination. When determining the effectiveness of a physical activity intervention, it is crucial to monitor how much physical activity is being performed, both within and outside of the administered program. Both Porock et al.'s (2000) and Headley et al.'s (2004) studies had significant missing data from patient-reported logs of physical activities (32, 50); it is not clear in either study as to the percentage of participants receiving the intended intervention. Oldervoll et al.'s study (2006) did

not report any method of assessing concurrent physical activity outside of the program (49), which contributes to the likelihood for contamination.

II-3.4. Primary and Secondary Outcomes of Included Studies

All 6 studies had either incomplete data reporting or missing data for one or more outcomes (see Tables II-3 and II-4). 3/6 (50%) of studies reported an increase in patient-reported quality of life scores, whereas in Headley et al.'s study (2004), the experimental group had a statistically significant slower decline in total well-being scores than the control group ($p=0.03$) (32). 2/6 (33%) of studies reported an increase in patient-reported physical function scores after their respective exercise interventions (26, 49), whereas Headley et al. (2004) showed no significant difference between groups at any time point (32). With respect to patient-reported fatigue, Headley et al. (2004) reported that the experimental group had a statistically significant slower rate of increase in fatigue ($p=0.01$) than the control group (32), whereas Oldervoll et al. (2006) demonstrated a borderline significant decrease in total fatigue subscale scores ($p=0.06$) (49). Similarly, Oldervoll et al. (2006) reported a statistically significant improvement pre- to post-intervention in the dyspnea subscore ($p=0.006$) (49).

Only the three included case reports assessed objective measures of physical fitness, and only one of the remaining studies assessed objective measures of physical function (see Table II-4). All three case reports observed an increase in work capacity and physical fitness measures post-exercise (26, 27, 34). Oldervoll et al. (2006) found a statistically significant improvement in the 6-minute walk ($p=0.007$)

and timed sit-to-stand ($p=0.001$) pre- to post-intervention, which was not seen in their patient-reported physical functioning outcome (49).

II-4. DISCUSSION

This systematic review summarizes the best available evidence of physical activity as a supportive care intervention in palliative cancer patients. The predominance of pilot and feasibility studies is reflective of the emerging nature of this research area. There is significant clinical heterogeneity in terms of study designs, participants and interventions among the 6 included studies. There is a wide variety of cancer diagnoses with differences in presence of metastases and concurrent therapy. There is variable reporting of specifics of the physical activity interventions administered, including frequency, intensity and duration. Due to this widespread diversity, quantitative comparisons between the included studies are not possible and thus only qualitative assessment is appropriate.

The development of any new research area begins with pilot studies, and the current state of evidence of physical activity interventions in palliative cancer patients appears to be following this natural evolution. The objective of these primary studies was not to establish efficacy, but rather to determine whether palliative cancer patients were able to tolerate physical activity interventions, and whether it was feasible to conduct these interventions in this frail population. While precluding the ability to generalize findings across this patient population, the use of small sample sizes are often inherent in gathering pilot data. While methodological quality assessment is a fundamental component of systematic reviews in general, it may not

be merited at this primary stage of research development, given the difficulties of applying the same methodologic criteria to feasibility studies as to efficacy trials.

Nevertheless, there are promising findings from these preliminary studies of physical activity interventions in palliative cancer patients. Although incomplete data reporting and missing data were common throughout the 6 included studies, the majority of participants were able to tolerate various physical activity interventions. The sole RCT showed a statistically significant slower rate of decline in total well-being, as well as a statistically significant slower rate of increase in total fatigue, between treatment and control groups (32). The two single group pre- to post-intervention trials demonstrated trends of improvement in patient-reported QoL, fatigue and physical functioning (49, 50). Three case reports show improvement in selected outcomes (26, 27, 34). Overall, these primary studies do indicate that select palliative cancer patients are able to complete physical activity interventions, and that at least some of these patients report improvement in supportive care outcomes post-intervention.

It is clear, however, that more feasibility studies are required in order to advance this emerging field of research. Although it is encouraging that select palliative cancer patients are able to tolerate physical activity, which subgroups of this population would most benefit from these interventions is still unknown. Moreover, the characteristics differentiating palliative cancer patients who are interested and able to participate in physical activity interventions, from those who are not, require further definition. The 6 included studies employed a broad range of both patient-reported and objective measures of supportive care outcomes, many of

which have not been previously tested or validated in palliative cancer populations; further studies are needed to develop and refine standardized outcome assessments for these physical activity interventions, in order to facilitate inter-trial comparison.

Most importantly, none of the studies reported assessing the physical activity needs, interests and preferences of palliative cancer patients prior to developing their physical activity interventions. In addition, none of the studies reported assessing the underlying physical activity behavior or determinants of this population. The primary aim of palliative care is to maximize QoL, thus identifying the unique priorities and preferences of palliative cancer patients is a critical first step towards this goal. Designing an intervention based on the patients' identified interests and needs may therefore optimize recruitment and adherence rates, and potentially increase efficacy with respect to supportive care outcomes. Clearly, future pilot studies which elicit the specific physical activity behavior, determinants, interests and preferences of palliative cancer patients are warranted prior to developing any physical activity intervention for this population.

The strength of this systematic review lies in the comprehensiveness of the search strategy, involving multiple electronic databases from a variety of disciplines, and extensive handsearching of reference lists and recent conference proceedings, thus minimizing the impact of publication bias. A potential limitation of this review was the restriction of participant definition by clinician-estimated life expectancy, which was not consistently documented throughout the studies. Further feasibility studies are needed to substantiate preliminary findings and further advance this emerging area of research. Consensus is required to develop common definitions for

palliative cancer populations, interventions and outcomes in order to validate findings, justify interpretations and make meaningful recommendations to patients and their families.

Figure II-1: Study Flowchart

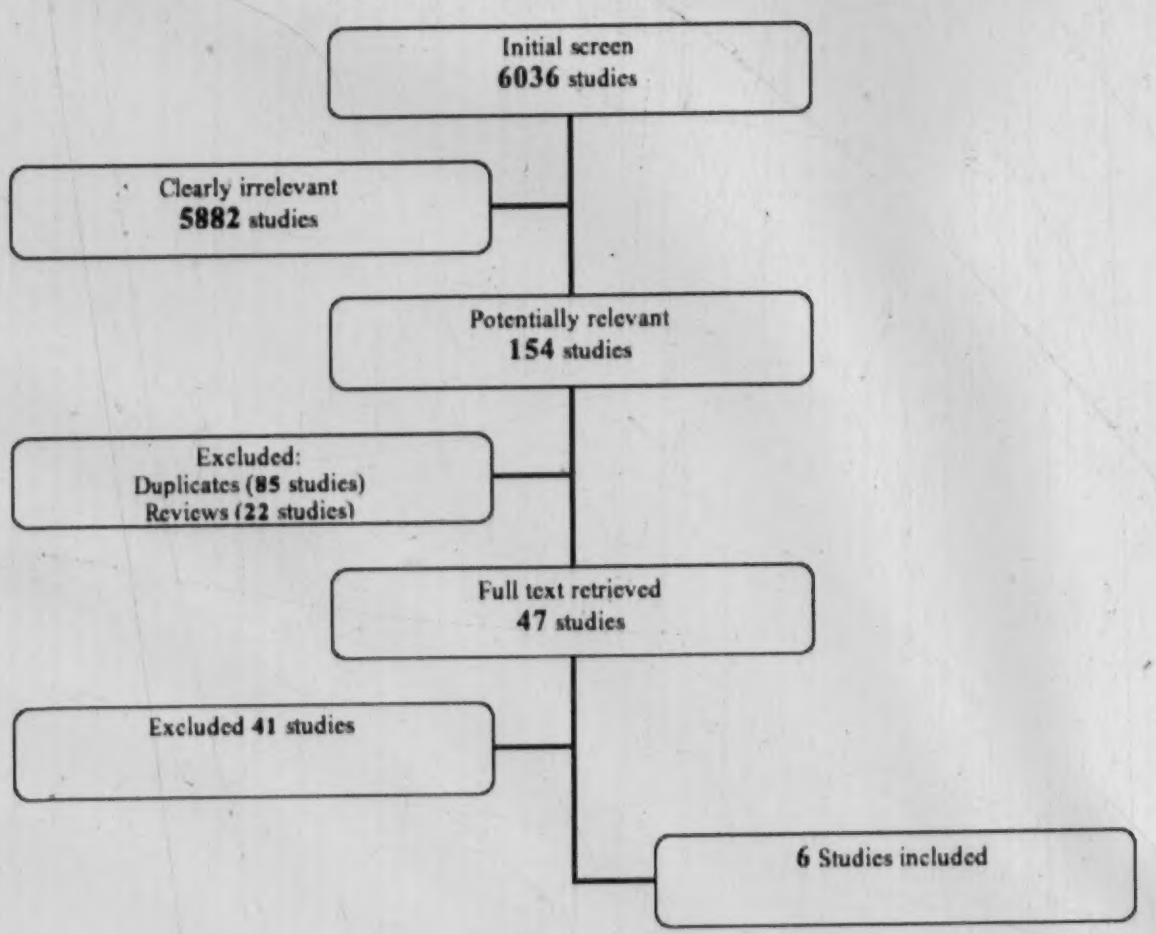

Table II-1: Characteristics of studies examining physical activity interventions in palliative cancer patients

Study	Features	Participants	Diagnoses	Intervention	Outcomes	Comments
Porock, 2000 (Australia)	Unsupervised home-based physical activity program in home hospice care patients	9 patients 3 male, 6 female Mean age 59.87 years (SD 9.77)	Bowel (n=4) Pancreas (n=2) Melanoma (n=1) Breast (n=1) Oral (n=1) Metastases (n=7) Active RT (n=1) Active chemo (n=2)	Individualized "Duke Energizing Exercise Plan" with range of physical activities throughout the day, frequency and duration set according to Winningham's half rule of thumb for 28 days.	1) Fatigue via MFI 2) Anxiety and Depression via HADS 3) Symptom Distress via McCorkle and Young's SDS 4) QoL via Graham and Longman's QoL scale	Single group pre-post intervention study. No staging information available. Incomplete data for HADS, adherence and withdrawals.
Crevenna, 2003 (*Wien Med Wschr*) (Austria)	Supervised aerobic exercise program during palliative thalidomide therapy	1 man, age 55 years old	Advanced hepatocellular cancer with lung and brain metastases	1) Bicycle ergometer cycling with workload systematic increase to maintain training HR at 60% of maximum workload of first symptom-limited exercise test. 60 min per session, 2 sessions per week for 6 weeks.	1) Symptom-limited ergometric bicycle exercise test: peak work capacity, endurance capacity and HR 2) 6-minute walk 3) Grimsby's self-reported physical performance questionnaire 4) QoL via SF-36 5) Self-reported benefit in physical performance, mental state, satisfaction and QoL	Case report. Partially reported baseline performance status. No adverse events reported. 100% compliance with training sessions. Participant commented on "being persistently and positively motivated by the physicians".

(SD = standard deviation; RT = radiotherapy; MFI = Multidimensional Fatigue Inventory; HADS = Hospital Anxiety and Depression Scale; SDS = Symptom Distress Scale; QoL = Quality of Life; HR = heart rate; SF-36 = Short Form 36 Survey)

Table II-1 continued: Characteristics of studies examining physical activity interventions in palliative cancer patients

Study	Features	Participants	Diagnoses	Intervention	Outcomes	Comments
Crevenna, 2003 (*Support Care Cancer*) (Austria)	Supervised aerobic exercise program during palliative chemotherapy (gemcitabine, epirubicin, paclitaxel) and palliative radiotherapy	1 female, age 48 years old	Advanced breast cancer with lung, liver and bone metastases	1) Bicycle ergometer cycling with workload increased to maintain training HR at 60% of maximum workload of first symptom-limited exercise test. 60 min per session, 3 sessions per week for 52 weeks.	1) Symptom-limited ergometric bicycle exercise test: VO_2max, peak work capacity, and HR 2) Lung function via respiratory quotient 3) QoL via SF-36 4) Self-reported benefit in physical performance, mental state, fatigue, sleep, satisfaction and QoL	Case report. Baseline performance status not reported. No adverse events reported. Participant attributed benefit to persistent and positive motivation by the physicians.
Kelm, 2003 (Germany)	Supervised whole body strength and endurance training during post-op intrahepatic chemotherapy	1 man, age 58 years old	Rectal adenocarcinoma (pT3N0M1) with liver metastases	1) Strength training machines at 40-60% of 1-repetition maximum up to 5 series of 20 repetitions. 2) Treadmill/ bicycle/ upper body ergometer 10 mins each with resistance and speed controlled to HR between 130-150bpm. 6-weeks postop and every 2 weeks between chemotherapy cycles for total of 13 weeks	1) Upper extremity and Lower extremity strength: 1RM 2) Endurance by reduction in HR and lactate concentration 3) Lung function by FEV_1, FVC and VC 4) QoL by GIQLI score 5) Immune function by NK cell count	Case report. Unknown baseline performance status. Unable to determine whether functional gains secondary to post-op recovery or intervention.

(VO_2max = peak oxygen uptake; HR = heart rate; GIQLI = Gastrointestinal Quality of Life Index; QoL = Quality of Life; SF-36 = Short Form 36 Survey; 1-RM = 1-repetition maximum; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; VC = vital capacity; NK = natural killer cell)

Table II-1 continued: Characteristics of studies examining physical activity interventions in palliative cancer patients

Study	Features	Participants	Diagnoses	Intervention	Outcomes	Comments
Headley, 2004 (USA)	Unsupervised home-based seated exercise program in stage IV breast cancer patients receiving chemotherapy	38 women Mean age 51 years (SD 9.43)	Stage IV breast cancer (n=38)	Seated exercise program using Armchair Fitness: Gentle Exercise video, 30 minutes per session, 3 sessions per week for 12 weeks	1) Fatigue and QoL via the FACIT-F 2) Perceived intensity via the Borg Rating of Perceived Exertion scale	Randomized controlled longitudinal trial. Incomplete data for adherence, intensity and frequency of activity.
Oldervoll, 2005, 2006 (Norway)	Supervised group exercise program in palliative patients from outpatient clinic and hospice	34 patients 15 males, 19 females Mean age 65 years (SD 11.5) Mean KPS 83 (SD 13.2)	Gastrointestinal (n=16) Breast (n=5) Genitourinary (n=5) Lung (n=1) Miscellaneous (n=7) Metastases (n=27) Active chemo (n=9) Active hormone therapy (n=3)	Group exercise program (3-8 patients per group) with personalized circuit training stations focused on UE/LE muscle strength, standing balance and aerobic endurance with 50 minutes per session, 2 sessions per week for 6 weeks.	1) Physical performance via 6-minute walk, timed sit-to-stand, functional reach 2) Fatigue via FQ 3) QoL via EORTC QLQ-C30	Single group pre-post intervention study. No progression of workload reported. Adherence rate to exercise sessions 10.6/12. 46% attrition rate.

(SD = standard deviation; FACIT-F = Functional Assessment of Chronic Illness Therapy – Fatigue Version IV; KPS = Karnofsky Performance Score; UE/LE = Upper extremity / Lower extremity; FQ = Fatigue Questionnaire; QoL = Quality of Life; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire)

Table II-2: Methodological Quality Assessment of studies examining physical activity interventions in palliative cancer patients

Study	Selection Bias	Allocation Bias	Confounders	Blinding	Data Collection Methods	Withdrawals and Dropouts
Porock, 2000 (Australia)	Weak	Weak	Weak	Weak	Strong	Strong
Crevenna, 2003 (*Wien Med Wschr*) (Austria)	Weak	Weak	Weak	Weak	Strong	Strong
Crevenna, 2003 (*Support Care Cancer*) (Austria)	Weak	Weak	Weak	Weak	Strong	Strong
Kelm, 2003 (Germany)	Weak	Weak	Weak	Weak	Strong	Strong
Headley, 2004 (USA)	Weak	Moderate	Weak	Weak	Strong	Weak
Oldervoll, 2005, 2006 (Norway)	Moderate	Weak	Weak	Weak	Strong	Weak

Table II-3: Patient-reported outcomes of studies examining physical activity interventions in palliative cancer patients

Study	Quality of Life (tool / score)	Physical Function (tool / score)	Fatigue (tool / score)	Symptoms (tool / score)
Porock, 2000 (Australia)	Graham & Longman's Scale Mean QoL rating: 5.3 (Day 0) 6.1 (Day 7) 6.6 (Day 14)	None reported	Incomplete data for all time points	Incomplete data
Crevenna, 2003 (*Wien Med Wschr*) (Austria)	SF-36 General health perception subscale: Pre: 65, Post: 62	SF-36 Physical functioning subscale: Pre:65, Post:85	SF-36 Vitality/fatigue subscale: Pre:25, Post:50	SF-36 Pain subscale: Pre: 22, Post: 41
Crevenna, 2003 (*Support Care Cancer*) (Austria)	None reported	None reported	None reported	SF-36 Incomplete data
Kelm, 2003 (Germany)	GIQLI Pre:106, Post:129 +21.6% difference	None reported	None reported	None reported
Headley, 2004 (USA)	FACIT-F Total scores: t[49]=2.31; **p=0.0254** Experimental group decline in total-wellbeing slower rate than in control group	FACIT-F Functional well-being subscale: no significant difference between groups at any time point	FACIT-F Fatigue subscale: t[49]=2.78; **p=0.0078** Experimental group decline in fatigue slower rate than in control group	None reported
Oldervoll, 2006 (Norway)	EORTC QLQ-C30 Global quality of life subscale: Pre:61(21), Post:64(20) **p=0.26**	EORTC QLQ-C30 Physical functioning subscale: Pre:65(20), Post:67(22) **p=0.62**	Fatigue Questionnaire Total fatigue subscale: Pre:17.5(4.7), Post:15.5(5.8) **p=0.06** Mental fatigue subscale: Pre:5.3(1.7), Post:5.1(2.0) **p=0.42** Physical fatigue subscale: Pre:12.2(3.6), Post:10.4(4.1) **p=0.04**	EORTC QLQ-C30 Nausea/vomiting: Pre:18(25), Post:14(19) **p=0.26** Pain: Pre:41(35), Post:37(34) **p=0.36** Dyspnea: Pre:42(33), Post:30(31) **p=0.006** Appetite loss: Pre:37(38), Post:28(35) **p=0.07**

(QoL = quality of life; SF-36 = Short Form 36 Survey; GIQLI = Gastrointestinal Quality of Life Index; FACIT-F = Functional Assessment of Chronic Illness Therapy – Fatigue Version IV; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire)

Table II-4: Objective outcomes of studies examining physical activity interventions in palliative cancer patients

Study	Physical Function (tool / score)	Physical Fitness (tool / score)
Porock, 2000 (Australia)	None reported	None reported
Crevenna, 2003 (*Wien Med Wschr*) (Austria)	None reported	Heart rate at sub-maximal workload: Pre:135, Post:103 -23.7% Peak work capacity: Pre:114, Post:137 +20.2% Endurance capacity: Pre:69%, Post:84% +20.3%
Crevenna, 2003 (*Support Care Cancer*) (Austria)	None reported	Heart rate at maximal workload: Pre:178, Post:191 +7.3% Peak oxygen uptake: Pre:20.3, Post:31 +52.7% Peak work capacity: Pre:129, Post:175 +35.7%
Kelm, 2003 (Germany)	Incomplete data	Heart rate: -10% Lactate concentration: -21.5% Force expiratory volume: Pre:2.48, Post:2.80 +12.9% Forced vital capacity: Pre:3.27, Post:3.64 +11.3% Inspiratory vital capacity: Pre:3.32, Post:3.61 +9.0%
Headley, 2004 (USA)	None reported	None reported
Oldervoll, 2006 (Norway)	6 minute walk: Pre:481(144), Post:510(156) **p=0.007** Sit to stand: Pre:5.1(2.3), Post:4.1(1.4) **p=0.001** Functional reach: Pre:30.4(6.9), Post:32.8(8.3) **p=0.07**	None reported

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III. CHAPTER THREE

"Physical Activity as a Supportive Care Intervention in Palliative Cancer Patients: A Pilot Survey"

III-1. INTRODUCTION

Cancer is one of the leading causes of morbidity and mortality, with an estimated 7.6 million deaths from cancer worldwide (1). Although advances in therapy have extended the chronicity of this disease, approximately two-thirds of individuals diagnosed with cancer will not be cured (2). Living longer with incurable cancer is accompanied by disease progression and escalating symptom burden, both of which negatively impact the patient's overall quality of life (3).

Optimizing quality of life is the central aim of palliative care, which is the holistic management of active, progressive, advanced disease for whom prognosis is limited (4). Inherent in this goal is the multidisciplinary approach to the treatment of disease-associated symptoms, such as pain and fatigue, in order to alleviate suffering. Although the principles of palliative care can be applied throughout the cancer trajectory, palliation becomes the sole focus at the end stages of cancer, wherein both physical and psychological symptoms are the most distressing to patients and their families (5).

Cancer-related fatigue and loss of physical function have been prioritized by advanced cancer patients as being among their top three most distressing symptoms (6). In combination with progressive muscle weakness and cachexia, the inability to perform activities of daily living independently adds to the distress level and disease burden for cancer patients (7). Associations between progressive debility and poorer social and psychological well-being have re-directed emphasis towards examining quality of life interventions that maintain patient's mobility for as long as possible (8).

Recent meta-analyses have shown that physical activity can improve several aspects of physical and psychological well-being that contribute to quality of life in cancer patients (9), but few studies have focused on palliative cancer patients (10). Courneya and Friedenreich (2007) have proposed the *Physical Activity and Cancer Control* (PACC) framework with the aim of organizing and stimulating physical activity research across the cancer trajectory; feasibility studies have demonstrated that at least some end-stage cancer patients are willing and able to participate in physical activity interventions (10).

Most recently, Oldervoll et. al. (2006) conducted a pilot uncontrolled trial of a 6-week group exercise intervention in 34 advanced cancer patients with a clinician-estimated life expectancy of between 3 and 12 months (11); despite showing improvements in both objective physical functioning, patient-reported emotional functioning and physical fatigue, the authors concluded that future research should be directed at "earlier physical exercise habits…to see if this has significance for whether palliative patients want to participate in an exercise intervention" (12). In our systematic review of physical activity as a supportive care intervention in palliative cancer patients, none of the included studies reported assessing for either interests or preferences of this population prior to the development of their interventions (unpublished data).

Knowledge of the specific physical activity interests and preferences of palliative cancer patients is critical in designing an effective intervention (13). Designing a physical activity intervention on this basis may thereby enhance recruitment, adherence rates, and optimize potential benefits and desired outcomes. To

the best of our knowledge, no study has examined the specific interests and preferences for physical activity in palliative cancer patients, nor has any study explored if there is an association between patient-reported physical activity and quality of life in this population. The primary objective of this study was to examine the physical activity interests and preferences of palliative cancer patients, and to determine any associations between patient-reported physical activity and quality of life, physical functioning and symptoms.

III-2. METHODS

III-2.1. Setting and Participants

The study was conducted at the Department of Symptom Control and Palliative Care, Cross Cancer Institute and the Regional Palliative Home Care program in Edmonton, Canada. Ethical approval for the study was received from the Health Research Ethics Board of the University of Alberta and the Research Ethics Board of the Alberta Cancer Board (see Appendix III-4). All participants were diagnosed with progressive, incurable, and locally recurrent or metastatic cancer. Eligibility criteria also included: 1) 18 years of age or older; 2) able to understand, provide written informed consent in, and speak English;
3) cognitive ability to participate (defined as a normal Folstein's Mini Mental Status Score for patient's age and education level (14)); and 4) clinician-estimated life expectancy of between 3 and 12 months.

Participants were ineligible if they presented with: 1) Any absolute contraindications to physical activity (15); and 2) Palliative Performance Scale level of 30% or less (16) . Eligible participants were required to read and sign a consent form

(see Appendix III-2), which detailed the right to withdraw, confidentiality, and the risks and benefits of participating in the study.

III-2.2. Design and Recruitment

The study was a cross-sectional survey conducted by face-to-face interview. Potential participants were recruited from the Department of Symptom Control and Palliative Care, Cross Cancer Institute (n=26) or from the Regional Palliative Home Care Program (n=24) from November 2006 to May 2007. In the palliative home care setting, consecutive patients admitted to the program were approached by nurse case managers to request permission to be contacted and assessed for study eligibility. A recruitment letter (see Appendix III-3) was also mailed to the patient who was then asked to contact the study coordinator if interested in participating in the study. At the Cross Cancer Institute, potential participants were identified by physician and nurse consultants from consecutive referrals to the Department of Symptom Control and Palliative Care through the Multidisciplinary Pain and Symptom Outpatient Clinic and the inpatient consultation service. Also at the Cross Cancer Institute, a recruitment handout was distributed to consecutive patients admitted through the outpatient radiotherapy units and outpatient lung clinics, and if patients were interested in participating in the study, patients consented to be contacted by the study coordinator by returning the handout with their contact information.

III-2.3. Survey Instrument (see Appendix III-1)

Patient-reported quality of life was assessed by the McGill Quality of Life Questionnaire (MQOL) (17) and patient symptoms were assessed by the Edmonton Symptom Assessment Scale (ESAS) (18). The MQOL covers five domains, including

physical symptoms, physical well-being, psychological, existential, and support, via 16 items in addition to one global quality of life (QOL) question. The MQOL has been found to be comprehensive, widely tested and valid across end-of-life populations (19). The ESAS covers 9 items, including physical, psychological and well-being subscales, and has been also widely tested and validated in palliative populations (20). Both MQOL and ESAS items have been modified for this study to incorporate open-ended questions with respect to impact on physical function and activity.

Physical activity behavior was assessed by four questions modified from concepts and short items drawn from the Physical Activity Scale for the Elderly (PASE), which requires participants to recall their most common physical activities, including frequency, intensity and duration, performed over the past week (21). For the purposes of the study, physical activity was defined as any bodily movement produced by the skeletal muscles that results in a substantial increase in energy expenditure over resting levels (22); this definition was explained to the participant prior to beginning the questionnaire. The PASE was developed for assessment of community-dwelling, older adults and has been widely used and validated in various clinical populations, including end stage renal patients (23); given the symptom burden of palliative cancer patients, the PASE was selected for its sensitivity in assessing activity in frail populations (24).

Physical functioning was assessed by the abbreviated version of the Late-Life Function and Disability Instrument (LLFDI) (25). The LLFDI is comprised of both a function component, which examines lower and upper extremity function, and a

disability component, which examines the limitation in performing both instrumental and basic activities of daily living. For the purposes of this study, only the function component of the abbreviated LLFDI was used. The LLFDI has been widely used and validated in elderly populations (26).

Exercise program preference was assessed by seven open short items and four closed short items drawn from previous research in cancer populations (13, 27). These items were designed to elicit the preferred specifics of a physical activity program. Participants were asked to select one category from each of the following specific items: company (ie. alone, with caregiver/spouse, with family/friends, with other cancer patients, no preference), location (ie. at home, at a hospital-based center, at a cancer center, at a local fitness center, no preference), time of day (morning, afternoon, evening, no preference), and duration (less than 10 minutes, 10-20 minutes, 20-30 minutes, over 30 minutes, not at all). In an open question format, participants were asked to indicate the following specific items: the meaning of physical activity to the participant, the current importance of being physically active to the participant, current interest in a physical activity program, self-assessment of current ability to participate in a physical activity program, frequency of physical activity program desired, favorite physical activity and the type of physical activity most interested in currently.

Medical and demographic information were collected using self-report measures and via medical chart review. This information consisted of demographic variables including age, height, weight, marital status, education, income, employment status and ethnicity, and medical variables including months since diagnosis, type and

duration of adjuvant treatment, current medications, smoking and alcohol status, medical co-morbidities, current palliative performance status level and actual date of death.

III-2.4. Sample Size Calculation and Statistical Analysis

As with our previous studies examining associations between exercise and quality of life in early-stage cancer patients (28, 29), the sample size calculation was based on Cohen's guideline for effect sizes of 0.20 = small, 0.50 = medium, and 0.80 = large. When comparing two means with 25 participants per group, we can detect a standardized effect size of 0.70 in the various outcomes (quality of life, physical activity) with a power of 80% and a two-tailed alpha value of <0.10; hence our accrual goal was 50 participants in total.

Given that there are no established physical activity level recommendations for advanced cancer patients (30), participants were divided into two categories based on a roughly median split on their most common self-reported physical activity over the past week: (1) walking ≥ 30 minutes per day; and (2) walking < 30 minutes per day. Participants were also divided into two categories based on their self-reported total physical activity over the past week: (1) total physical activity ≥ 60 minutes per day; and (2) total physical activity < 60 minutes per day.

Pilot data were analysed using SPSS version 15.0 software (SPSS Inc., Evanston, Illinois). In order to determine the physical activity interests and preferences of the sample, frequency counts and percentages were calculated. Chi-square analysis was performed to examine potential associations between physical activity preferences and the following demographic, medical and physical activity variables: age (< 60

years versus ≥ 60 years), gender (male versus female), body mass index (normal/underweight versus overweight/obese), palliative performance scale level (< 60% versus ≥ 60%), total number of comorbidities (< 2 versus ≥2), cancer diagnosis (lung cancer versus other), site of study entry (Cross Cancer Institute versus Regional Palliative Home Care), survival from time of interview to time of death (< 90 days versus ≥ 90 days), walking (< 30 minutes per day versus ≥ 30 minutes per day), and total physical activity (< 60 minutes per day versus ≥ 60 minutes per day).

Differences in patient-reported quality of life, physical function and symptoms between participants in the two physical activity categories were tested using independent t-tests. Effect sizes (*d*) were computed by dividing the mean difference between categories by the pooled standard deviation (31). To examine potential confounding variables, analyses were repeated using analysis of covariance (ANCOVA) to adjust for the following demographic and medical variables: age (< 60 years versus ≥ 60 years), gender (male versus female), marital status (single versus partnered), number of metastatic sites (< 2 metastatic sites versus ≥ 2 metastatic sites), and current chemotherapy (yes versus no). In order to test for potential moderators of the associations between physical activity and total MQOL scores, total LLFDI scores, ESAS pain scores and ESAS fatigue scores, ANOVAs were performed with age (< 60 years versus ≥ 60 years), gender (male versus female), body mass index (normal/underweight versus overweight/obese), palliative performance scale level (< 60% versus ≥ 60%), total number of comorbidities (< 2 versus ≥2), cancer diagnosis (lung cancer versus other), and survival from time of interview to time of death (< 90 days versus ≥ 90 days) as potential moderators. With the same covariates

as the main effects analyses, the moderator analyses were repeated using ANCOVAs to control for potential confounding variables. Probabilities of less than 0.05 and Cohen's effect size $d \geq 0.35$ (small-medium) were interpreted as significant.

III-3. RESULTS

III-3.1. Sample Characteristics

Recruitment began November 2006 at the Cross Cancer Institute and January 2007 at the Regional Palliative Home Care Program, and ended May 2007 at both sites. Figure III-1 shows the flow of participants through the study. 47/244 (19%) screened home care patients consented to being contacted by the study coordinator, and 23/47 (49%) patients were eligible for and recruited to the study. One home care patient was recruited through the mail-out recruitment letter of invitation. 8/119 (7%) screened outpatient radiotherapy unit patients consented to being contacted by the study coordinator through the recruitment handout, with 1/8 (13%) patients eligible for and recruited to the study. 2/62 (3%) screened outpatient lung clinic patients consented to being contacted by the study coordinator through the recruitment handout, with 1 patient eligible for and recruited to the study. The estimated accrual rate from the Department of Symptom Control and Palliative Care was 24 of 92 potentially eligible participants (26%). Of all patients who contacted the study coordinator, the most common reason for declining to participate was severe fatigue (n=15).

III-3.2. Demographic and Medical Characteristics

As of January 21/08, 38/50 (76%) study participants were deceased, with a median duration of 104 days from the date of conducting survey to the date of death.

Of those participants who were deceased, the maximum duration from time of survey to time of death was 356 days, whereas the minimum duration was 23 days. When combining the deceased participants into the total sample, 16/50 (32%) participants had an actual survival of < 90 days, and 34/50 (68%) participants had an actual survival of ≥ 90 days from time of survey to time of death.

Of the participants who reported walking less than 30 minutes per day over the past week (n=25), 68% (17/25) were deceased with a mean survival of 108 days. Of the participants who reported walking 30 minutes or more per day over the past week (n=25), 84% (21/25) were deceased with a mean survival of 127 days. Of the participants who reported total physical activity levels of less than 60 minutes per day over the past week (n=25), 80% (20/25) were deceased with a mean survival of 113 days. Of the participants who reported total physical activity levels of 60 minutes or more per day over the past week (n=25), 72% (18/25) were deceased with a mean survival of 125 days.

To examine the representativeness of the sample, participants recruited from the Cross Cancer Institute (n=26) were compared with participants recruited from the Regional Palliative Home Care program (n=24) across demographic and medical variables. The only significant difference was observed for gender ($p < 0.05$), with participants recruited from the Cross Cancer Institute being more likely to be male than those recruited from the Regional Palliative Home Care program (55.6% versus 21.7%).

The demographic and medical characteristics of participants are presented in Tables III-1 and III-2 respectively. In summary, the mean age of participants was 61.5

± 13.1 years, 60% were female (n=30), 42% were married or common law (n=21), 50% completed Grade 12 education or higher (n=25), and the overwhelming majority were not employed (n=46, 92%). The average body mass index was 24.4 (SD 5.9, n=50). Of the list provided, lung cancer was reported as the most common diagnosis (n=15, 30%). The majority of participants had a palliative performance scale level of 60% (n=25, 50%). The most common site of metastasis was bone (n=22, 44%) and lung (n=22, 44%), with 54% of participants having two or more metastatic sites concurrently (n=27). 34% of participants were receiving chemotherapy at the time of the survey (n=17).

III-3.3. Physical Activity Behavior, Quality of Life, Physical Function and Symptoms

Table III-3 presents descriptive data for physical activity behavior, quality of life, physical function and symptoms of all participants (n=50). In summary, the most common type of self-reported physical activity over the past week was walking, with a mean duration of 351 ± 331 (SD) minutes; 50% of participants reported walking 30 minutes or more per day over the past week (n=25). The mean duration of total physical activity over the past week was 740 ± 625 (SD) minutes, with 50% of participants reporting that they engaged in physical activity for 60 minutes or more per day over the past week (n=25). The mean total MQOL score was 5.7 ± 0.8 (SD), wherein a total MQOL score of 10 represents the highest patient-reported quality of life. The mean total LLFDI score was 37.3 ± 10.2 (SD), wherein a total LLFDI score of 75 represents the lowest patient-reported physical functioning. Overall, the highest

rated symptom reported by participants was fatigue, with a mean ESAS score of 5.2 ± 2.3 (SD), wherein an ESAS score of 10 represents the worst possible fatigue.

III-3.4. Physical Activity Preferences

Details of the participants' physical activity preferences are presented in Table III-4. Overall, 92% of participants reported (ie. yes or maybe) that they would be interested in a physical activity program at the time of survey, with 92% of participants reporting (ie. yes or maybe) that they felt able to participate in a physical activity program. More than half of the participants (54%) preferred to participate in physical activity alone. Furthermore, 84% of participants indicated that they would prefer to begin a physical activity program in their own homes. Approximately equal proportions of participants reported that they preferred to exercise in the morning (40%) and once per day (42%). Preferring to perform a physical activity program of less than 20 minutes in duration was endorsed by 66% of participants. The majority of participants (64%) reported that walking was their favorite physical activity, with 72% of participants indicating that walking was the type of physical activity that they were most interested in at the time of survey. Resistance training ranked second in the type of physical activity that participants were most interested in at the time of survey (12%).

III-3.5. Associations between Demographic, Medical and Physical Activity Variables and Physical Activity Preferences

Chi-square analyses indicated that being overweight or obese was associated with being less likely to prefer to perform a physical activity program alone ($\chi^2 = 5.15$, $p < 0.05$), and with being more likely to prefer to perform a physical activity

program in the morning ($\chi^2 = 4.08$, $p < 0.05$). Second, having a diagnosis of lung cancer was associated with being less likely to report walking as the favorite physical activity ($\chi^2 = 3.97$, $p < 0.05$) and with being less likely to report walking as the type of physical activity that participants were most interested in at the time of survey (Fisher's exact, $p < 0.05$). The remaining demographic and medical variables (ie. age, gender, total number of comorbidities, site of study entry, palliative performance scale level and survival from time of survey to time of death) and physical activity behavior over the past week did not influence physical activity preferences in this sample.

III-3.6. Associations between Physical Activity Behavior and Quality of Life

Data for the primary outcomes of patient-reported quality of life are presented in Tables III-5 and III-6. Given that higher MQOL scores are indicative of higher patient-reported quality of life, there is an overall pattern favoring the higher walking and physical activity categories over their lower counterparts for patient-reported quality of life. In our unadjusted analyses, participants who reported walking 30 minutes or greater per day over the past week also reported higher existential subscores (mean between group difference = 0.8, 95% CI = 0.0 to 1.5; p=0.045), higher support subscores (mean between group difference = 0.7, 95% CI = 0.1 to 1.4; p=0.027) and higher total scores (mean between group difference = 0.5, 95% CI = 0.0 to 0.9; p=0.046) of the MQOL. Cohen's effect size *d* for these differences ranged from 0.58 to 0.65. These differences in quality of life did not change substantially after adjusting for the covariates of age (< 60 years versus ≥ 60 years), gender (male versus female), marital status (single versus partnered), number of metastatic sites ($<$ 2 metastatic sites versus ≥ 2 metastatic sites), and current chemotherapy (yes versus

no). For example, in our adjusted analysis participants who reported walking 30 minutes or greater per day over the past week, still reported higher total scores (mean between group difference = 0.4, 95% CI = 0.0 to 0.9; p=0.048) on the MQOL.

Similarly, participants who reported participating in physical activity for 60 minutes or more per day over the past week, also reported higher existential subscores (mean between group difference = 1.1, 95% CI = 0.4 to 1.8; p=0.002) on the MQOL; Cohen's effect size *d* for this difference was 0.90. This difference in quality of life remained after adjusting for the abovementioned potential covariates, with participants who reported participating in physical activity for 60 minutes or more per day over the past week, still reporting higher existential subscores on the MQOL (mean between group difference = 1.0, 95% CI = 0.2 to 1.8; p=0.011). Interestingly, participants who reported participating in physical activity for 60 minutes or more per day over the past week, also reported lower psychological subscores (mean between group difference = -1.3, 95% CI = -2.5 to -0.1; p=0.039) on the MQOL; in our adjusted analysis, however, this association was slightly reduced (mean between group difference = -1.2, 95% CI = -2.6 to 0.2; p=0.079).

III-3.7. Associations between Physical Activity Behavior and Patient-Reported Physical Functioning

Data for the secondary outcomes of patient-reported physical functioning are presented in Tables III-5 and III-6. Given that lower LLFDI scores are indicative of higher patient-reported physical functioning, upon comparison across categories of walking and total physical activity over the past week, there is an overall pattern favoring the higher activity categories over their lower counterparts for patient-

reported physical functioning. Although not statistically significant, our unadjusted analysis showed a pattern towards association between participants who reported walking 30 minutes or greater per day over the past week and lower advanced lower extremity function subscores (mean between group difference = -2.1, 95% CI = -5.1 to 0.9; p=0.172) and lower total scores (mean between group difference = -3.3, 95% CI = -9.1 to 2.5; p=0.261) on the LLFDI. Cohen's effect size *d* for these differences were -0.39 and -0.32, respectively. These differences in patient-reported physical functioning did not change after adjusting for the covariates of age (< 60 years versus ≥ 60 years), gender (male versus female), marital status (single versus partnered), number of metastatic sites (< 2 metastatic sites versus ≥ 2 metastatic sites), and current chemotherapy (yes versus no).

This overall pattern of association was also reflected in the total physical activity categories, although they did not reach statistical significance: participants who reported engaging in physical activity for 60 minutes or more per day over the past week also reported lower advanced lower extremity function subscores (mean between group difference = -2.5, 95% CI = -5.5 to 0.5; p=0.096) and lower total scores (mean between group difference = -1.8, 95% CI = -7.7 to 4.0; p=0.530). Interestingly, participants who reported engaging in physical activity for 60 minutes or more per day over the past week, also reported higher upper extremity function subscores (mean between group difference = 1.5, 95% CI = -0.8 to 3.7; p=0.195) on the LLFDI, although this was not a statistically significant association. Adjusting for the abovementioned potential covariates did not substantially alter these results.

III-3.8. Associations between Physical Activity Behavior and Patient-Reported

Symptoms

Data for the secondary outcomes of patient-reported symptoms are presented in Tables III-5 and III-6. Given that lower ESAS scores are indicative of improvement in patient-reported symptoms, there is an overall pattern favoring the higher walking and physical activity categories over their lower counterparts for patient-reported symptoms. Although not statistically significant, our unadjusted analysis showed a pattern towards association between participants who reported walking 30 minutes or greater per day over the past week and lower fatigue scores (mean between group difference = -0.7, 95% CI = -2.1 to 0.6; p=0.273) on the ESAS; Cohen's effect size *d* for this difference was -0.31. The patient-reported symptom on ESAS that most closely approached statistical significance in terms of an association with patient-reported walking was lower nausea scores (mean between group difference = -1.2, 95% CI = -2.4 to 0.0; p=0.056). These differences in patient-reported symptoms did not change after adjusting for the covariates of age (< 60 years versus ≥ 60 years), gender (male versus female), marital status (single versus partnered), number of metastatic sites (< 2 metastatic sites versus ≥ 2 metastatic sites), and current chemotherapy (yes versus no).

With respect to the total physical activity categories, there was more variability apparent in associations between total physical activity behavior over the past week and patient-reported symptoms, although none achieved statistical significance. In particular, participants who reported engaging in physical activity for 60 minutes or more per day over the past week, also reported higher fatigue scores (mean between group difference = 0.1, 95% CI = -1.2 to 1.4; p=0.895) and lower pain scores (mean

between group difference = -.05, 95% CI = -1.9 to 0.9; p=0.443) on the ESAS; Cohen's effect size *d* for these differences were 0.04 and -0.22, respectively. The patient-reported symptom on ESAS that most closely approached statistical significance in terms of an association with patient-reported total physical activity was lower anxiety scores (mean between group difference = -1.3, 95% CI = -0.1 to 2.6; p=0.064), with Cohen's effect size *d* of 0.54. Adjusting for the abovementioned potential covariates did not substantially alter these results.

III-3.9. Moderator Analysis of Associations between Physical Activity Behavior, Quality of Life, Physical Functioning and Symptoms

Examination of potential moderators revealed that the variables of age (< 60 years versus ≥ 60 years), gender (male versus female), body mass index (normal/underweight versus overweight/obese), palliative performance scale level (< 60% versus ≥ 60%), total number of comorbidities (< 2 versus ≥2), cancer diagnosis (lung cancer versus other), and survival from time of interview to time of death (< 90 days versus ≥ 90 days) did not moderate the association between physical activity behavior and total MQOL scores, total LLFDI scores, ESAS pain scores and ESAS fatigue scores. Covarying for age (< 60 years versus ≥ 60 years), gender (male versus female), marital status (single versus partnered), number of metastatic sites (< 2 metastatic sites versus ≥ 2 metastatic sites), and current chemotherapy (yes versus no) did not substantially alter the results of our moderator analyses.

III-4. DISCUSSION

The purposes of this study were to elicit the physical activity interests and preferences of palliative cancer patients, and to determine any associations between

patient-reported physical activity and quality of life, physical functioning and symptoms. The data indicate that participation in physical activity was low in this sample, with walking being the most common type of physical activity performed by the participants. An overwhelming majority of palliative cancer patients in this sample were interested and felt able to participate in a physical activity program, with the majority of participants indicating a preference to perform physical activity alone and in their own homes. There was a strong association between higher patient-reported walking and total physical activity levels and higher quality of life, particularly within the existential component of the MQOL. Overall, these findings provide strong rationale for the development of a physical activity program tailored to palliative cancer patients as a supportive care intervention.

III-4.1. Physical Activity Behavior and Preferences

In terms of prevalence of physical activity, there are no current physical activity level recommendations for advanced cancer patients (30) with which to compare our results. In a pilot accelerometry study of 20 ambulant outpatients with advanced upper gastrointestinal cancer receiving palliative chemotherapy, Dahele et al. (2007) showed that the median time spent stepping approached 600 minutes over a one week period (32); these findings are in contrast with our study, wherein the median time spent walking was 225 minutes in total over the past week via patient self-report. Comparison between objective and self-report measures of physical activity is difficult given the tendency of patients to over-estimate physical activity levels on self-report (33). Given that their median Eastern Cooperative Oncology Group (ECOG) performance status was 1 (32), Dahele et al.'s (2007) participants

were presumably much earlier in the cancer trajectory, and hence more likely to be ambulatory, than those in our sample. Despite these differences, however, it is clear that the amount of physical activity undertaken by the participants in our sample is very low; this low level of physical activity is not unexpected given the progressive fatigue, cachexia and debility that patients encounter at the end stages of cancer (8).

The results of our study are consistent with previous research eliciting exercise preferences in other groups of cancer patients. Overall, 92% of participants in our study reported (ie. yes or maybe) that they would be interested in and that they felt able to participate in a physical activity program. Similarly, in a survey of 431 non-Hodgkin's lymphoma patients, Vallance et al. (2006) reported that 81% of respondents indicated that they would possibly be interested in, and 85% of respondents indicated that they would possibly be able to participate in an exercise programme (34). In another survey of 386 endometrial cancer patients, Karvinen et al. (2006) reported that 77% of participants indicated possible interest in doing an exercise program, with 82% feeling able or likely able to actually participate in an exercise program (35). In contrast to these previous survey studies, our participants are at the end stages of cancer, with progressive tumor and symptom burdens; deterioration in physical condition and functioning have been identified by palliative cancer patients as among the top reasons for desiring death (36). The hope of potentially slowing or delaying this physical decline may explain the strong desire to participate in a physical activity program, as reported by our participants.

Another finding in our study was the strong preference to engage in physical activity alone, which was endorsed by 54% of participants. Similarly, in a survey of

307 prostate, breast, colorectal and lung cancer patients, Jones and Courneya (2002) reported that 44% of respondents preferred to exercise alone (37). This response coincides with evidence that older non-cancer individuals prefer exercise interventions targeted at the individual level, rather than in a group format (38, 39). Although worsening debility in cancer patients has been associated with increasing dependency on others (40), the desire to perform physical activity independently may supercede the need for social support in our sample of palliative cancer patients.

Compared to other cancer populations, the appetite for home-based physical activity programs is particularly strong. The significance of performing physical activity alone is reinforced by the fact that 84% of participants preferred to engage in physical activity at home. This response is more than double that of a recent survey of 106 primary brain cancer patients, in which Jones et al. (2006) reported that 40% of respondents preferred to exercise at home (13), and nearly double that of Vallance et al.'s study (2006), wherein 43% of their sample of non-Hodgkin's lymphoma patients preferred a home-based exercise program (34). In a qualitative study of 180 palliative cancer patients, Tang (2003) showed that 87% of participants indicated that they wished to receive end-of-life care in their own homes (41); the home setting has been identified as critical for maintaining a patient's dignity and autonomy, and has been considered one of the benchmarks of the quality of palliative care (42).

As well as being the most common modality of physical activity performed by our participants over the past week, walking was identified as the preferred modality of physical activity by the majority of our sample. This finding is coherent with both Jones et al. (2006) and Vallance et al.'s (2006) previous studies, wherein 53% and

81% of brain cancer patients and non-Hodgkin's lymphoma patients, respectively, preferred to walk for exercise (13, 34). For the participants in our sample, walking may be the ideal physical activity because of the minimal equipment required and the ability to perform this modality in their preferred home environment. Home-based walking programs have been examined in various early stage breast cancer populations, with beneficial effects on cancer-related fatigue and physical functioning (43-45). Considering the progressive fatigue and physical debility that occurs at the end stages of cancer, a home-based walking intervention may be optimal for adherence and supportive care outcomes in our palliative cancer population.

12% of our participants reported resistance training as the second most preferred type of physical activity, with an equal proportion indicating no preference. Furthermore, 66% of respondents preferred to engage in less than 20 minutes of physical activity per session, with 56% preferring to participate in up to 3 physical activity sessions per week. These responses coincide with Drouin et al.'s (2006) model of exercise prescription in individuals with low functional status: in order to maintain physical functioning and prevent deconditioning, patients who are bedbound or experience fatigue on mild exertion may benefit from short sessions of low-intensity activity several times per week (46). Taken together, these results reinforce the significance of eliciting the specific programming interests and preferences of participants before initiating a physical activity intervention.

After exploring potential associations between the demographic, medical, behavioral variables and physical activity preferences in our sample, chi square analyses yielded a small number of inconsistent associations. These results are in

contrast to previous studies showing the uniform influence of age, gender and exercise behavior in modifying exercise preferences across various early stage cancer populations (34, 37). Our findings are not surprising given our small sample size of 50 participants; it is evident that larger studies are required to confirm these results and further delineate potential interactions between demographic, medical, behavioral variables and physical activity preferences in this palliative cancer population.

Our study is the first to directly examine the physical activity interests and preferences of palliative cancer patients. Our study is also the first to examine potential associations between demographic, medical, behavioral variables and physical activity preferences in this population. A third study strength is the tracking of participant survival from time of survey to time of death, thus confirming the clinician-estimated prognosis of our participants. Limitations of this study include the small sample size and the measurement of preferences using single-item scales which have not been validated in the palliative cancer population. Another limitation is the potential for selection bias, in that palliative cancer patients who were more interested in physical activity were probably more likely to participate in the study.

The results of this study have several practical implications for clinicians in palliative oncology. Our results demonstrate that palliative cancer patients are very interested in and feel able to participate in a physical activity intervention. Moreover, the majority of participants in our sample indicated that they would like to participate in physical activity alone and at home, with a strong preference for walking as their modality of choice. Compared to previous research in early stage cancer populations, palliative cancer patients have distinct and varied interests and preferences which

should be carefully considered in the design and development of future physical activity interventions.

III-4.2. Associations between Quality of Life, Physical Functioning, Symptoms and Physical Activity Behavior

We report the associations between patient-reported QoL, physical functioning, symptoms and physical activity behavior in a sample of palliative cancer patients. Our results showed a strong association between participants who reported walking 30 minutes or greater per day over the past week and existential, support and total MQOL scores. Similarly, there was a very strong association between participants who reported engaging in physical activity for 60 minutes or more per day over the past week and existential MQOL scores.

We can assume that the mean differences between walking categories ranging from 0.45 to 0.76 points for the existential, support and total MQOL scores are clinically meaningful based on various indices. Firstly, in a study evaluating differences in quality of life scores from different instruments in laryngeal cancer patients, Ringash et al. (2007) concluded that the positive MID was approximately 5% of the maximal instrument score; in comparison with previous research, this rule of thumb appeared to be relatively consistent across patient diagnoses and various assessment tools for both quality of life and functional status (47). Using this method of estimation would place the MID of the MQOL at 0.5 points, within which our results represent a meaningful difference in quality of life. Secondly, Sloan et al. (2005) deemed that a conservative estimate of clinically meaningful effect size would be 0.50 standard deviations (48), and the observed difference in total MQOL scores

between walking groups in our study was 0.53 standard deviations. Finally, in a recent study evaluating the efficacy of a psychosocial supportive intervention in 60 older palliative home care patients, Duggleby et al. (2007) reported a mean difference of 0.62 points as being a significant improvement in total MQOL scores (49), which compares favorably with the observed differences in our study.

This positive association between patient-reported physical activity and quality of life is consistent with previous research in early stage cancer populations (29, 50, 51), and is unique in comparison to previous studies in more advanced cancer populations. Dahele et al.'s (2007) accelerometry study showed no correlation between average number of steps taken per day and global QOL scores of the EORTC QLQ-C30 in advanced gastrointestinal cancer patients undergoing chemotherapy (32); our participants, however, were less physically active and, as evident by their median survival of 104 days, were further along the cancer trajectory. In a pilot study of a group exercise intervention in 34 mixed cancer patients with an estimated life expectancy of between 3 and 12 months, Oldervoll et al. (2006) reported a significant improvement in both the emotional and social functioning subscores ($p < 0.01$) of the EORTQ QLQ-C30, although the global QoL and physical functioning score remained unchanged (11). In our sample, higher physical symptom and physical well-being MQOL subscores were associated with both patient-reported walking and total physical activity over the past week, although these associations were not statistically significant.

The existential MQOL subscore was the only outcome measure that had a statistically significant positive association with both patient-reported walking and

total physical activity over the past week. The existential MQOL subscore measures the patient's concerns about their personal meaning in life, and has been established as a fundamental determinant of quality of life in palliative cancer patients (19). Contemplating the meaning of life and death becomes more prevalent at the end stages of cancer, particularly as physical debility increases (52). In two studies of 420 mixed cancer patients and 167 breast cancer patients, Jim et al. (2007) reported that the association between impairments in physical functioning and distress were mediated by the individual's perceived meaning in life (53). This evidence linking existential concerns and physical functioning may explain the strong positive association between patient-reported physical activity and the existential MQOL subscore in our participants, as they may perceive being physically active with delaying or slowing functional impairments.

With respect to patient-reported physical functioning, there was an overall pattern favoring the higher activity categories over their lower counterparts. In particular, Cohen's effect size *d* for advanced lower extremity functioning subscores ranged from -0.39 to -0.48 for patient-reported walking and total physical activity levels over the past week, respectively. The lack of statistical significance may be explained by our use of the abbreviated LLFDI instrument, which may not have had sufficient sensitivity to discriminate functional differences within a palliative cancer population experiencing inevitable physical decline. In a recent systematic review, Jordhoy et al. (2007) showed that physical functioning is a neglected dimension in palliative care quality of life measures, and that there is little consensus as to how physical functioning should be assessed or what components of physical functioning

should be elicited in palliative cancer patients (8). Clearly future research is required into standardized tools of physical functioning that are validated for this population.

Likewise, there was an overall pattern of improvement in patient-reported symptoms and increasing patient-reported walking and total physical activity over the past week. Although not statistically significant, our results demonstrated decreased ESAS fatigue scores with increased patient-reported walking, and decreased ESAS pain scores with increased patient-reported physical activity. These findings are in contrast to Oldervoll et. al. (2006), who reported significant improvement in dyspnea ($p < 0.01$), with a pattern of improvement in EORTC QLQ-C30 fatigue, pain and nausea scores in 34 advanced cancer patients post-exercise intervention (11). In our sample, the variability in direction of response seen in patient-reported symptoms between patient-reported physical activity categories may be explained by our use of the ESAS, which assesses each symptom using a single item visual analogue scale (18); given that symptoms such as cancer-related fatigue can have multiple physical and psychological etiologies, multidimensional symptoms may require the use of multidimensional assessment tools in order to elucidate potential associations (55). Future studies may benefit from the selection of a multidimensional instrument for more in-depth exploration of the patient-reported symptom as the primary outcome.

Our exploratory analysis showed that neither age, gender, body mass index, palliative performance scale level, total number of comorbidities, cancer diagnosis, nor survival moderated the association between physical activity behavior and total MQOL scores, total LLFDI scores, ESAS pain scores and ESAS fatigue scores. Our findings are not surprising given our small sample size of 50 participants; it is evident

that larger studies are required to confirm these results and further delineate potential interactions between demographic and medical variables with physical activity behavior and patient-reported quality of life, physical functioning and symptoms in this palliative cancer population.

Due to the observational nature of this study, one cannot infer that the strong association between physical activity and quality of life in palliative cancer patients is a cause-effect relationship, or if other variables are responsible for this association. Despite adjusting for multiple potential covariates, there may be other factors involved and that were not measured in our sample. Other limitations of this study include the small sample size, although our study is the largest to date on physical activity in palliative cancer patients. Finally, we relied on self-reported physical activity, which has not been validated in a palliative cancer population. Future studies combining both objective measurements and patient-reported assessments of physical activity levels should be conducted in the palliative cancer population.

Nonetheless, this study carries a number of significant clinical implications for palliative care providers. Our results clearly show a positive association between patient-reported physical activity and quality of life in palliative cancer patients. In particular, there is a very strong association between higher patient-reported physical activity levels and higher existential well-being, which has been prioritized as among the fundamental determinants of quality of life by palliative cancer patients (56). Furthermore, our findings demonstrate an overall pattern of improvement in patient-reported physical functioning and symptoms, and increased patient-reported physical activity levels. Given the benefits in supportive care outcomes from physical activity

interventions in other cancer populations (9, 57, 58), these results lend impetus to the initiation of a physical activity intervention trial in palliative cancer patients.

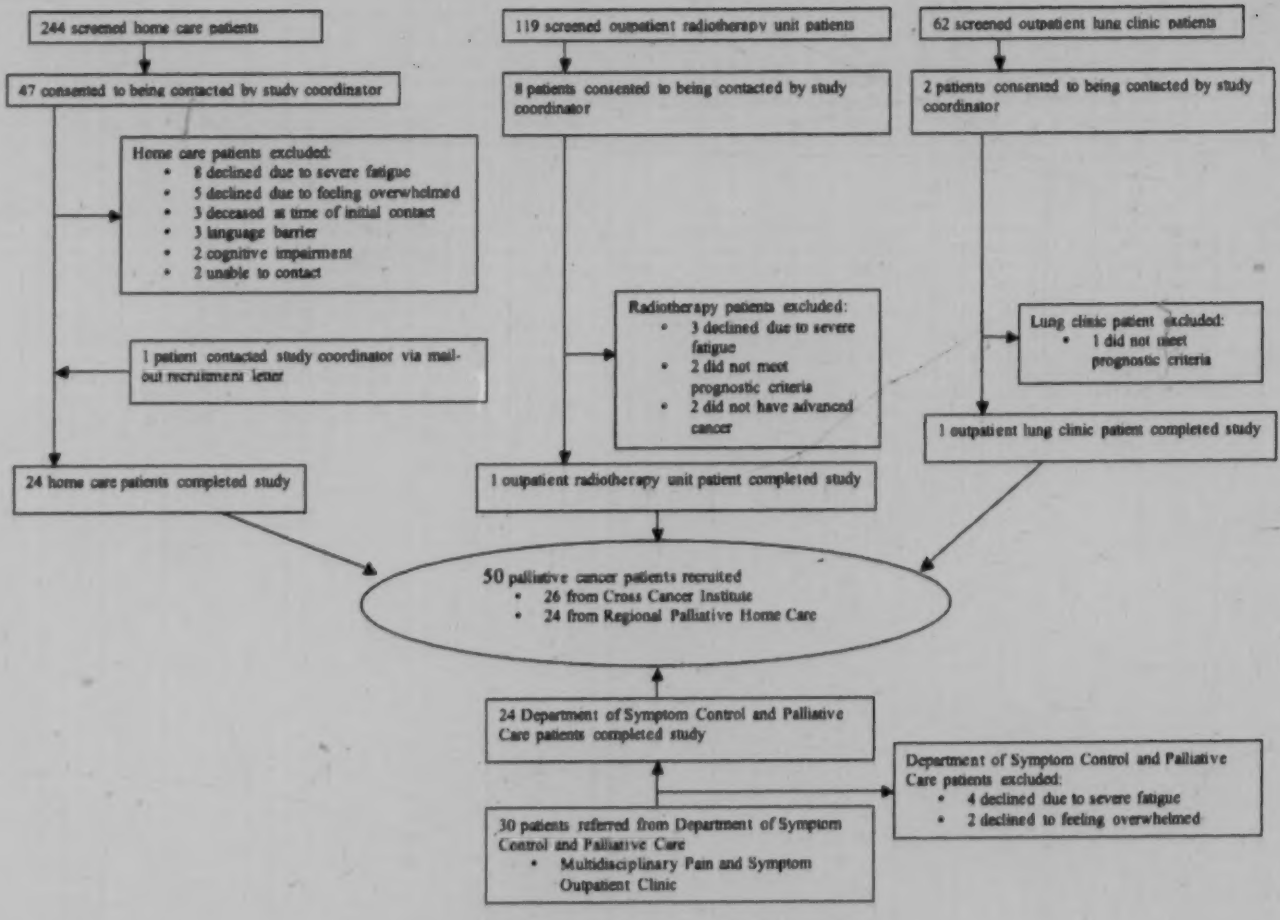
244 screened home care patients
47 consented to being contacted by study coordinator
Home care patients excluded:
• 8 declined due to severe fatigue
• 5 declined due to feeling overwhelmed
• 3 deceased at time of initial contact
• 3 language barrier
• 2 cognitive impairment
• 2 unable to contact
1 patient contacted study coordinator via mail-out recruitment letter
24 home care patients completed study
119 screened outpatient radiotherapy unit patients
8 patients consented to being contacted by study coordinator
Radiotherapy patients excluded:
• 3 declined due to severe fatigue
• 2 did not meet prognostic criteria
• 2 did not have advanced cancer
1 outpatient radiotherapy unit patient completed study
62 screened outpatient lung clinic patients
2 patients consented to being contacted by study coordinator
Lung clinic patient excluded:
• 1 did not meet prognostic criteria
1 outpatient lung clinic patient completed study
50 palliative cancer patients recruited
• 26 from Cross Cancer Institute
• 24 from Regional Palliative Home Care
24 Department of Symptom Control and Palliative Care patients completed study
Department of Symptom Control and Palliative Care patients excluded:
• 4 declined due to severe fatigue
• 2 declined to feeling overwhelmed
30 patients referred from Department of Symptom Control and Palliative Care
• Multidisciplinary Pain and Symptom Outpatient Clinic

Figure III-1. Flow of Participants through the Study

Table III-1: Demographic characteristics of participants (n=50)

Demographic Variables	N (%)
Age	
< 60 years	21 (42%)
≥ 60 years	29 (58%)
Mean ± SD	61.5±13.1
Gender	
Male	20 (40%)
Female	30 (60%)
Marital Status	
Married/Common law	21 (42%)
Other	29 (58%)
Education	
Completed Grade 12 or higher	25 (50%)
Lower than Grade 12	25 (50%)
Annual family income	
< $40,000	8 (16%)
≥ $40,000	42 (84%)
Employment status	
Employed full/part time	4 (8%)
Not employed	46 (92%)

Table III-2: Medical characteristics of participants (n=50)

Medical Variables	N (%)
Body mass index	
Underweight	8 (16%)
Normal	17 (34%)
Overweight	17 (34%)
Obese	8 (16%)
Mean±SD	24.4±5.9
Number of comorbidities	
< 2	29 (58%)
≥ 2	21 (42%)
Most common comorbidities	
Hypertension	17 (34%)
Arthritis	12 (24%)
Dyslipidemia	11 (22%)
COPD	6 (12%)
Smoking status	
Never smoked	20 (40%)
Ex-smoker	22 (44%)
Current smoker	8 (16%)
CAGE	
0	48 (96%)
1	2 (4%)
Cancer Diagnosis	
Lung	15 (30%)
Genitourinary	11 (22%)
Breast	8 (16%)
Gastrointestinal	8 (16%)
Hematological	4 (8%)
Head and neck	2 (4%)
Other	2 (4%)
PPS level	
40%	2(4%)
50%	2(4%)
60%	25(50%)
70%	19(38%)
80%	2(4%)
Sites of metastases	
Bone	22(44%)
Lung	22(44%)
Liver	11(22%)
Brain	5(10%)
Other	18(36%)

(CAGE = screen for alcohol abuse, rated from 0 to 4 for a maximum total score of 4; PPS = Palliative Performance Scale)
(Underweight: BMI < 18.5; Normal: 18.5-25; Overweight: 25-30; Obese > 30)

Table III-2 continued: Medical characteristics of participants (n=50)

Medical Variables	N (%)
Number of metastastic sites	
≤1	23 (46%)
≥2	27 (54%)
Treatment received	
Surgery	
Never	23 (46%)
Completed	27 (54%)
Chemotherapy	
Never	15 (30%)
Completed	18 (36%)
Current	17 (34%)
Radiation	
Never	19 (38%)
Completed	28 (56%)
Current	3 (6%)
Recurrence	
Never	34 (68%)
≥1	16 (32%)

Table III-3: Descriptive Statistics for Physical Activity Behavior, Quality of Life, Physical Function and Symptoms (n=50)

Variable	Mean ± SD
Physical Activity over the past week	
Walking minutes	351 ± 331
Housework minutes	271 ± 367
Stair climbing minutes	48 ± 126
Miscellaneous minutes	70 ± 267
Total physical activity minutes	740 ± 625
McGill Quality of Life Questionnaire	
Physical symptom subscale (0-10)	4.4 ± 1.2
Physical well-being subscale (0-10)	5.2 ± 1.7
Psychological subscale (0-10)	3.0 ± 2.2
Existential subscale (0-10)	7.4 ± 1.4
Support subscale (0-10)	8.7 ± 1.2
Total score (0-10)	5.7 ± 0.8
Late Life Function and Disability Instrument	
Basic lower extremity functioning subscale (5-25)	9.6 ± 3.7
Advanced lower extremity functioning subscale (5-25)	18.2 ± 5.3
Upper extremity functioning subscale (5-25)	9.4 ± 4.0
Total function score (15-75)	37.3 ± 10.2
Edmonton Symptom Assessment Scale	
Pain	3.3 ± 2.5
Fatigue	5.2 ± 2.3
Nausea	1.2 ± 2.2
Depression	1.8 ± 2.2
Anxiety	2.4 ± 2.4
Drowsiness	3.3 ± 2.8
Appetite	4.3 ± 2.7
Feeling of wellbeing	3.9 ± 2.0
Shortness of breath	3.0 ± 2.8

(MQOL: maximum score of 10 represents highest patient-reported quality of life; LLFDI: maximum score 25 represents lowest patient-reported physical functioning; ESAS: maximum score of 10 represents worst possible symptom)

Table III-4. Descriptive statistics for physical activity preferences of study participants (n=50)

Preference Variable	N (%)
Is being physically active important to you now?	
Yes	47(94%)
No	3(6%)
Are you interested in a physical activity program now?	
Yes	39(78%)
No	4(8%)
Maybe	7(14%)
Do you think you would be able to participate in a physical activity program now?	
Yes	29(58%)
No	4(8%)
Maybe	17(34%)
If you were to begin a physical activity program, who would you like to participate with?	
Alone	27(54%)
With caregiver/spouse	5(10%)
With family/friends	3(6%)
With other cancer patients	0
No preference	15(30%)
If you were to begin a physical activity program, where would you like to participate?	
At home	42(84%)
At a hospital-based center	0
At a cancer center	0
At a local fitness center	0
No preference	8(16%)
If you were to begin a physical activity program, would you prefer to participate in the:	
Morning	20(40%)
Afternoon	16 (32%)
Evening	2(4%)
No preference	12(24%)
If you were to begin a physical activity program, how long do you think you would be able to participate?	
< 10 minutes	16(32%)
10 to 20 minutes	17(34%)
20 to 30 minutes	11(22%)
> 30 minutes	6(12%)
Not at all	0

Table III-4 continued. Descriptive statistics for physical activity preferences of study participants (n=50)

Preference Variable	N (%)
If you were to begin a physical activity program, how often would you be interested in participating?	
Once per week	2(4%)
2 to 3 times per week	26(52%)
Once per day	21(42%)
Other	1(2%)
What is your favorite physical activity?	
Walking	32(64%)
Resistance training	3(6%)
Gardening	2(4%)
Housework	1(2%)
Other	8(16%)
No preference	2(4%)
None	2(4%)
What type of physical activity would you be most interested in now?	
Walking	36(72%)
Resistance training	6(12%)
Housework	1(2%)
Other	1(2%)
No preference	6(12%)

Table III-5: Quality of life, physical functioning and symptom differences between participants reporting walking 30 minutes or more per day (n=25) and walking less than 30 minutes per day (n=25) over the past week

Variable	Walking < 30 min/day (Mean ± SD)	Walking ≥ 30 min/day (Mean± SD)	Between group difference Mean [95%CI]	F	Effect Size (d)	P
McGill Quality of Life Questionnaire						
Physical symptom (0-10)	4.2 ± 1.3	4.5 ± 1.1	0.2 [-0.5 to 0.9]	0.4	0.19	0.517
Physical well-being (0-10)	4.9 ± 1.6	5.5 ± 1.7	0.6 [-0.3 to 1.6]	1.8	**0.38**	0.183
Psychological (0-10)	3.1 ± 2.6	2.9 ± 1.8	-0.1 [-1.4 to 1.1]	0.0	-0.06	0.836
Existential (0-10)	7.1 ± 1.5	7.8 ± 1.1	0.8 [0.0 to 1.5]	4.3	**0.58**	**0.045**
Support (0-10)	8.3 ± 1.2	9.0 ± 1.1	0.7 [0.1 to 1.4]	5.2	**0.65**	**0.027**
Total score (0-10)	5.5 ± 0.9	6.0 ± 0.7	0.5 [0.0 to 0.9]	4.2	**0.59**	**0.046**
Late Life Function and Disability Instrument						
Basic lower extremity function (0-25)	9.7 ± 3.7	9.6 ± 3.7	-0.1 [-2.2 to 2.0]	0.0	-0.03	0.910
Advanced lower extremity function (0-25)	19.2 ± 5.7	17.2 ± 4.8	-2.1 [-5.1 to 0.9]	1.9	**-0.39**	0.172
Upper extremity function (0-25)	10.0 ± 4.2	8.9 ± 3.7	-1.1 [-3.4 to 1.2]	1.0	-0.28	0.331
Total function score (0-75)	39.0 ± 10.0	35.6 ± 10.3	-3.3 [-9.1 to 2.5]	1.3	-0.32	0.261

(Cohen's effect size $d \geq 0.35$, $p < 0.05$ highlighted in bold)
(MQOL: maximum score of 10 represents highest patient-reported quality of life; LLFDI: maximum score 25 represents lowest patient-reported physical functioning)

Table III-5 continued: Quality of life, physical functioning and symptom differences between participants reporting walking 30 minutes or more per day (n=25) and walking less than 30 minutes per day (n=25) over the past week

Variable	Walking < 30 min/day (Mean ± SD)	Walking ≥ 30 min/day (Mean± SD)	Between group difference Mean [95%CI]	F	Effect Size (d)	P
Edmonton Symptom Assessment Scale						
Pain (0-10)	3.1 ± 2.5	3.5 ± 2.4	0.4 [-1.0 to 1.8]	0.3	0.15	0.590
Fatigue (0-10)	5.6 ± 1.9	4.8 ± 2.7	-0.7 [-2.1 to 0.6]	1.2	-0.31	0.273
Nausea (0-10)	1.8 ± 2.7	0.6 ± 1.4	-1.2 [-2.4 to 0.0]	3.8	**-0.55**	0.056
Depression (0-10)	2.2 ± 2.7	1.4 ± 1.6	-0.8 [-2.1 to 0.5]	1.7	**-0.36**	0.204
Anxiety (0-10)	2.4 ± 2.5	2.4 ± 2.4	0.0 [-1.4 to 1.4]	0.0	-0.01	0.977
Drowsiness (0-10)	3.6 ± 2.6	3.0 ± 3.0	-0.6 [-2.2 to 1.0]	0.6	-0.22	0.450
Appetite (0-10)	4.7 ± 3.0	3.8 ± 2.5	-0.9 [-2.5 to 0.6]	1.5	-0.34	0.230
Feeling of wellbeing (0-10)	4.3 ± 1.8	3.5 ± 2.2	-0.9 [-2.0 to 0.3]	2.3	**-0.43**	0.138
Shortness of breath (0-10)	3.4 ± 3.1	2.6 ± 2.6	-0.8 [-2.4 to 0.8]	1.1	-0.30	0.297

(Cohen's effect size $d \geq 0.35$, $p < 0.05$ highlighted in bold)
(ESAS: maximum score of 10 represents worst possible symptom)

Table III-6: Quality of life, physical functioning and symptom differences between participants reporting total physical activity of 60 minutes or more per day (n=25) and total physical activity less than 60 minutes per day (n=25) over the past week

Variable	Physical activity < 60 min/day (Mean ± SD)	Physical activity ≥ 60 min/day (Mean± SD)	Between group difference Mean [95%CI]	F	Effect Size (d)	P
McGill Quality of Life Questionnaire						
Physical symptom (0-10)	4.3 ± 1.3	4.4 ± 1.1	0.2 [-0.5 to 0.9]	0.2	0.13	0.624
Physical well-being (0-10)	4.9 ± 1.5	5.4 ± 1.8	0.5 [-0.5 to 1.4]	1.0	0.28	0.320
Psychological (0-10)	3.6 ± 2.0	2.4 ± 2.2	-1.3 [-2.5 to -0.1]	4.5	**-0.60**	**0.039**
Existential (0-10)	6.9 ± 1.3	8.0 ± 1.2	1.1 [0.4 to 1.8]	10.3	**0.90**	**0.002**
Support (0-10)	8.6 ± 1.2	8.8 ± 1.2	0.2 [-0.5 to 0.9]	0.3	0.16	0.574
Total score (0-10)	5.7 ± 0.6	5.8 ± 1.0	0.1 [-0.3 to 0.6]	0.4	0.16	0.543
Late Life Function and Disability Instrument						
Basic lower extremity function (0-25)	10.0 ± 3.7	9.2 ± 3.7	-0.8 [-2.9 to 1.3]	0.6	-0.22	0.450
Advanced lower extremity function (0-25)	19.5 ± 4.7	17.0 ± 5.7	-2.5 [-5.5 to 0.5]	2.9	**-0.48**	0.096
Upper extremity function (0-25)	8.7 ± 3.4	10.2 ± 4.4	1.5 [-0.8 to 3.7]	1.7	**0.37**	0.195
Total function score (0-75)	38.2 ± 9.1	36.4 ± 11.3	-1.8 [-7.7 to 4.0]	0.4	-0.18	0.530

(Cohen's effect size $d \geq 0.35$, $p < 0.05$ highlighted in bold)
(MQOL: maximum score of 10 represents highest patient-reported quality of life; LLFDI: maximum score 25 represents lowest patient-reported physical functioning)

Table III-6 continued: Quality of life, physical functioning and symptom differences between participants reporting total physical activity of 60 minutes or more per day (n=25) and total physical activity less than 60 minutes per day (n=25) over the past week

Variable	Physical activity < 60 min/day (Mean ± SD)	Physical activity ≥ 60 min/day (Mean± SD)	Between group difference Mean [95%CI]	F	Effect Size (d)	P
Edmonton Symptom Assessment Scale						
Pain (0-10)	3.6 ± 2.6	3.0 ± 2.3	-0.5 [-1.9 to 0.9]	0.6	-0.22	0.443
Fatigue (0-10)	5.2 ± 2.4	5.3 ± 2.3	0.1 [-1.2 to 1.4]	0.0	0.04	0.895
Nausea (0-10)	1.3 ± 2.4	1.1 ± 2.0	-0.2 [-1.5 to 1.0]	0.1	-0.10	0.727
Depression (0-10)	2.2 ± 2.5	1.5 ± 1.9	-0.6 [-1.9 to 0.6]	1.1	-0.29	0.311
Anxiety (0-10)	1.7 ± 2.1	3.0 ± 2.6	-1.3 [-0.1 to 2.6]	3.6	**0.54**	0.064
Drowsiness (0-10)	3.3 ± 2.7	3.3 ± 2.9	0.0 [-1.6 to 1.6]	0.0	0.01	0.960
Appetite (0-10)	4.6 ± 3.0	3.9 ± 2.5	-0.6 [-2.2 to 1.0]	0.6	-0.23	0.431
Feeling of wellbeing (0-10)	4.0 ± 1.8	3.8 ± 2.3	-0.3 [-1.4 to 0.9]	0.2	-0.13	0.657
Shortness of breath (0-10)	3.0 ± 3.0	3.0 ± 2.7	0.0 [-1.6 to 1.7]	0.0	0.01	0.961

(Cohen's effect size $d \geq 0.35$, $p < 0.05$ highlighted in bold)
(ESAS: maximum score of 10 represents worst possible symptom)

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IV. CHAPTER FOUR

"Home-based physical activity program for palliative cancer patients: Three Case Reports"

IV-1. INTRODUCTION

Cancer is the leading life-threatening illness, responsible for one out of every eight deaths worldwide (1). Both tumor burden and anti-tumor therapies can cause significant morbidity in cancer patients; among the most common physical symptoms of cancer include pain, fatigue and cachexia, whereas psychological symptoms can include depression, anxiety and poor sense of well-being. As cancer progresses beyond the point of cure, the symptomatic burden becomes increasingly pronounced and the management of these symptoms becomes crucial towards maintaining quality of life (2).

According to the U.S. National Cancer Institute, palliative care plays a critical role in symptom management to improve the quality of life of cancer patients (3). Palliative care brings a multidisciplinary approach to the management of pain and other distressing symptoms, wherein both pharmacological and non-pharmacological therapies are used with the focus of improving overall well-being (4). Although the principles of palliation can be applied throughout the cancer trajectory, the majority of cancer patients who receive palliative care are in the last months, weeks or days of life (5).

Among the most common distressing symptoms facing end stage cancer patients is loss of physical function (6). The underlying etiology of loss of physical function is multifactorial, with increasing cancer-related fatigue, progressive muscle wasting and generalized debility all contributing to this phenomenon (7). Not only does loss of physical function impede the patient's ability to perform activities of daily

living, but increasing physical dependence on caregivers and loved ones for support causes an additional emotional and psychological burden on the patient as well (8). The desire of advanced cancer patients to keep mobile is fundamentally linked to the desire to remain as independent as possible, and hence maintain their overall quality of life.

Increasing attention has been given to physical activity as a quality of life intervention in cancer patients (9). Although recent meta-analyses have determined that physical activity interventions can improve cancer-related fatigue and physical function outcomes in early stage cancer patients (10, 11), these benefits have not been established for patients at the end stages of cancer. In their proposed *Physical Activity and Cancer Control* (PACC) framework, Courneya and Friedenreich (2007) have identified the emergence of feasibility studies within the cancer control category of palliation (12); in our recent systematic review, there is preliminary evidence that select advanced cancer patients are willing and able to participate in a physical activity intervention, with positive benefit on supportive care outcomes (unpublished data).

Recently, Oldervoll et al. (2005) conducted a prospective phase II pilot study to examine the effects of a structured physical activity program on thirty-four advanced cancer patients with clinician-estimated survival between 3 and 12 months (13). 63% of the incurable cancer patients invited to the study were willing to participate in a physical activity intervention, and 54% of those who agreed to participate actually completed the intervention. Patients who did not want to participate, however, identified limitations of fatigue, lack of mobility, and the burden of physically getting to the hospital gym where the group exercise intervention took

place. The authors concluded that these limitations "might indicate a need for specially tailored interventions…in the form of home-based exercises adjusted for the individual patient" (14).

In clinical practice, there is no currently recommended home-based physical activity program that has been validated for the palliative cancer population. Porock et al. (2000) conducted a pilot study of nine home care hospice cancer patients who were administered a home-based program based on the Duke Energizing Exercise Plan, with a range of different physical activities prescribed according to the patient's individual condition and tolerability; despite the trend towards increased quality of life scores, it was unclear if the program took the participants' exercise preferences or interests into account, and the authors concluded that the optimal type of physical activity program for this population is still unknown (15).

We recently completed a pilot survey of fifty palliative cancer patients with a median survival of 104 days from time of survey to time of death; 92% of participants reported that they would be interested in and able to participate in a physical activity program (unpublished data). Moreover, 84% of participants indicated a preference for a home-based physical activity program, with 54% of participants preferring to participate in physical activity alone. Walking and resistance training were the top two modalities of physical activity endorsed by our participants, with 56% preferring to participate in up to 3 physical activity sessions per week. These findings demonstrate the unique and varied physical activity interests and preferences of palliative cancer patients, and highlight the fact that careful consideration of these preferences are

warranted in the design of physical activity programs in order to optimize adherence and supportive care outcomes.

To the best of our knowledge, no study has developed or tested a physical activity intervention for palliative cancer patients using their identified programming interests and preferences. Based on our preliminary survey data, the primary objective of this study was to examine the initial development and feasibility testing of a home-based physical activity program in palliative cancer patients. We present three case reports on a home-based physical activity program that incorporates knowledge of the specific physical activity interests and preferences of palliative cancer patients, in order to determine intervention feasibility and preliminary effects on supportive care outcomes.

IV-2. METHODS

IV-2.1. Setting and Participants

The study was conducted at the Department of Symptom Control and Palliative Care, Cross Cancer Institute and the Regional Palliative Home Care program in Edmonton, Canada. Ethical approval for the study was received from the Health Research Ethics Board of the University of Alberta and the Research Ethics Committee of the Alberta Cancer Board (see Appendix IV-6). All participants were diagnosed with progressive, incurable, and locally recurrent or metastatic cancer. Eligibility criteria also included: 1) 18 years of age or older; 2) able to understand, provide written informed consent in, and speak English; 3) cognitive ability to participate (defined as a normal Folstein's Mini Mental Status Score for patient's age

and education level (16)); and 4) clinician-estimated life expectancy of between 3 and 12 months.

Participants were ineligible if they presented with: 1) Any absolute contraindications to physical activity (17); and 2) Palliative Performance Scale level of 30% or less (18). Eligible participants were required to read and sign a consent form, which detailed the right to withdraw, confidentiality, and the risks and benefits of participating in the study.

IV-2.2. Experimental Design and Recruitment

The study was a pilot uncontrolled intervention trial to provide preliminary data on the feasibility and outcomes of a 6 week home-based physical activity program in advanced cancer patients. This design was selected over a randomized controlled trial at this stage because of the lack of previous evidence indicating the feasibility and acceptability of physical activity in this local palliative cancer population. Potential participants were recruited from the Department of Symptom Control and Palliative Care, Cross Cancer Institute or from the Regional Palliative Home Care Program from July to December 2007. In the palliative home care setting, consecutive patients admitted to the program were approached by nurse case managers to request permission to be contacted and assessed for study eligibility. A recruitment letter (see Appendix IV-5) was also mailed to the approved patient who was then required to contact the study coordinator if interested in participating in the study. At the Cross Cancer Institute, potential participants were identified by physician and nurse consultants from consecutive referrals to the Department of Symptom Control and Palliative Care through the Multidisciplinary Pain and Symptom Outpatient

Clinic. Also at the Cross Cancer Institute, a recruitment handout was distributed to consecutive patients admitted through the outpatient radiotherapy units, and if patients were interested in participating in the study, patients consented to being contacted by the study coordinator by returning the handout with their contact information.

IV-2.3. Overview of Physical Activity Intervention

Based on preliminary data from our pilot survey of palliative cancer patients, the majority of participants indicated walking and resistance training as their two most preferred modalities of physical activity, and identified home as their preferred location of physical activity program (unpublished data). We therefore adopted a home-based functional walking program, modified from a tailored exercise program described by Gardner et al. (2001) for the elderly (19). Modifications to the original functional walking program were drawn from Best-Martini et al.'s *Exercise for Frail Elders* (2003) (20) and review of the exercise oncology literature. This modified home-based functional walking program involves a walking plan and combination of muscle strengthening and balance retraining exercises to be individually prescribed in each person's own home. In a meta-analysis of randomized controlled trials using the home-based functional walking program in the elderly, Robertson et al. (2002) concluded that it was particularly effective in frail participants because of the reduction in fall-related injuries, and the increase in muscle strength and balance above the minimum required for basic and instrumental activities of daily living (21).

After providing written informed consent (see Appendix IV-4), participants completed a baseline survey questionnaire (see Appendix IV-1) by face-to-face interview, and performed baseline physical function tests. Based on the results of

baseline testing, participants were prescribed an individualized home-based functional walking program involving walking, muscle strengthening and balance retraining components (Table IV-1). All participants received hands-on supervision and instruction by a professional exercise therapist and/or study coordinator for the initial training session and thrice weekly home visits for the entire duration of the study. Participants were asked to wear an activPAL™ accelerometer (22) to monitor ambulatory activity levels for the duration of the study, as well as to record their activities in a daily logbook (see Appendix IV-3). After completion of the six week program, participants completed a post-intervention survey questionnaire by face-to-face interview, and physical function tests to monitor for changes.

IV-2.4. Specifics of Home-Based Functional Walking Program

For the 6-week long intervention period, the modified home-based functional walking program combined both aerobic and anaerobic components. The aerobic component required participants to perform daily walking, with duration and intensity individually prescribed based on the results of their baseline physical function testing. Because the activPAL™ accelerometers monitored stepping activity for the duration of the study, none of the aerobic walking sessions were supervised. For the anaerobic component, participants performed muscle strengthening and balance retraining exercises, three times per week on non-consecutive days. All anaerobic sessions were supervised by a professional exercise therapist and/or the study coordinator in the participants' homes. Any missed anaerobic sessions were not rescheduled, therefore the maximum number of prescribed anaerobic sessions was 18.

The mode, intensity (resistance) and duration of each anaerobic exercise were based on the results of the participant's baseline physical function testing as well as on Drouin's model (2006) of low-to-moderate intensity activity with the aim of maintaining physical function and preventing deconditioning (23). Variations on each anaerobic exercise were provided for increasing levels of difficulty and to allow for individual prescription. Ankle/wrist cuff weights and/or resistance bands were used to provide resistance during muscle strengthening and balance retraining exercises as individually prescribed. Depending on the participant's symptoms and overall condition, changes in number of exercises, sets and repetitions were made with the aim to progress to the desired exercise prescription as soon as safely possible. Five minutes of warm up and cool down exercises were performed before and after each anaerobic session. Further details of the modified home-based functional walking program are provided in Tables IV-1 and IV-2.

IV-2.5. Objective Assessment of Physical Functioning

Physical functioning was assessed both pre- and post-intervention by items drawn from the Seniors Fitness Test (SFT) (24), with the inclusion of a four-test balance scale described by Gardner et al. (2001) for assessment of impaired balance in the elderly (19). The purpose of the SFT is to measure basic physical function parameters associated with functional tasks and activities that are significant in the everyday living of older adults; it is comprised of 6 measures, the results of which are aimed to design individualized, targeted physical activity programs for clients (25). Both the four-test balance scale and the SFT have been widely used and validated in elderly populations (24, 26), and were selected for their sensitivity in assessing

physical functioning in frail populations. Grip strength was assessed using a handheld dynamometer. In addition to these standardized tests, the participant's height, weight and body mass index were measured. Blood pressure, heart rate and oxygen saturation were measured pre- and post-physical function testing. Further details of the objective physical function measures are provided in Table IV-3.

IV-2.6. Objective Assessment of Physical Activity

Physical activity was assessed using the *activ*PAL™ accelerometer, which records triaxial movement in the form of lying or sitting, quiet standing and stepping. The 20 gram, 35 x 53 x 7 millimeter unit is secured to the participant's anterior mid-thigh using an adherent hydrogel PALstickie™ and participants were asked to remove the units when bathing or showering, and replace once the underlying skin is dried. Participants were asked to wear the unit for one baseline week prior to initiation of the intervention, and for the 6-week duration of the program. In addition to cadence and number of steps taken, the intensity and volume of stepping is also recorded on a second-by-second basis. Thus the *activ*PAL™ system calculates the estimated energy expenditure by assigning an estimated energy cost in metabolic equivalents (METs) to each activity category. The *activ*PAL™ accelerometer has been validated in a number of clinical populations (22), and most recently has been tested in a pilot study of 20 advanced upper gastrointestinal cancer patients undergoing palliative chemotherapy (27).

IV-2.7. Survey Instrument (see Appendices IV-1 and IV-2)

Quality of life was assessed by the McGill Quality of Life Questionnaire (MQOL) (28). The MQOL covers five domains, including physical symptoms,

physical well-being, psychological, existential, and support, via 16 items in addition to one global quality of life (QoL) question. The MQOL has been found to be comprehensive, widely tested and valid across end-of-life populations (29).

Physical activity behavior was assessed by four questions modified from concepts and short items drawn from the Physical Activity Scale for the Elderly (PASE), which requires participants to recall their most common physical activities, including frequency, intensity and duration, performed over the past week (30). For the purposes of the study, physical activity was defined as any bodily movement produced by the skeletal muscles that results in a substantial increase in energy expenditure over resting levels (31). The PASE was developed for assessment of community-dwelling, older adults and has been widely used and validated in various clinical populations (32), including end stage renal patients (33); given the symptom burden of palliative cancer patients, the PASE was selected for its sensitivity in assessing activity in frail populations.

Patient-reported physical functioning was assessed by the abbreviated version of the Late-Life Function and Disability Instrument (LLFDI) (34). The LLFDI is comprised of both a function component, which examines lower and upper extremity function, and a disability component, which examines the limitation in performing both instrumental and basic activities of daily living. For the purposes of this study, only the function component of the abbreviated LLFDI was used. The LLFDI has been widely used and validated in elderly populations (35).

Patient-reported symptoms were assessed by the Edmonton Symptom Assessment Scale (ESAS) (36). The ESAS covers 9 items, including physical,

psychological and well-being subscales, and has been also widely tested and validated in palliative populations (37). In particular, fatigue was assessed by the Brief Fatigue Inventory, which is a nine-item self-report instrument designed for rapid and reliable assessment of cancer-related fatigue, and has been tested and validated in a variety of cancer populations (38). Hope was assessed by the Hope Differential-Short Instrument (HDS), which has been validated for use as a clinical tool for assessing hope in palliative care populations (39).

Program satisfaction was assessed by a combination of closed and open short items designed to elicit participant satisfaction with the administered intervention. Participants were asked to select one response on a sliding scale for each of the following categories: final impressions, perceived benefits and disadvantages, perceived barriers to participation during the program and in the future, degree of support received during the program, lessons learned from program, motivation and interest in pursuing a future physical activity program. In an open question format, participants were asked to comment on the following categories: length and content of questionnaire, program specifics and expertise, impressions of specific exercises and equipment, and suggestions for improvement.

Medical and demographic information were collected using self-report measures and via medical chart review. This information consisted of demographic variables including age, marital status, education, income, employment status and ethnicity, and medical variables including months since diagnosis, type and duration of adjuvant treatment, current medications, smoking and alcohol status, medical co-morbidities, current palliative performance status level and actual date of death.

IV-2.8. Sample Size Calculation and Statistical Analysis

For this single-factor repeated-measures design, our accrual goal was 30 participants to detect a change of 0.5 standard deviations (a medium effect size) in the various outcomes (physical functioning, quality of life, fatigue) with a power of 85% and a two-tailed alpha value of <0.05 (40). Participant characteristics and rates of recruitment, retention, adherence and safety were to be summarized using descriptive statistics. Planned statistical analysis included two-sided repeated measures t-tests of pre- to post-intervention changes in measured outcomes, adopting $p<0.05$ as the level of statistical significance.

IV-3. RESULTS

IV-3.1. Sample Characteristics and Recruitment

Accrual was stopped early after 9 recruited participants. There was slower than expected accrual and higher than expected attrition. As shown by Figure IV-1, 16% (10/61) of home care patients who consented to being contacted by the study coordinator, declined due to severe fatigue; 8% (5/61) of home care patients who consented to being contacted by the study coordinator, were recruited to the study. 30% (6/20) of Department of Symptom Control and Palliative Care patient referrals declined due to severe fatigue; 5% (1/20) of the remaining eligible Department of Symptom Control and Palliative Care patient referrals were recruited to the study. 20% (3/15) of outpatient radiotherapy unit patients who consented to being contacted by the study coordinator, did not meet inclusion criteria for the study because of out-of-town residence; 20% (3/15) of the remaining eligible outpatient radiotherapy unit patients were recruited to the study.

Of the 9 palliative cancer patients who consented to the study, 22% (2/9) of participants dropped out prior to baseline physical function testing because of admission to hospital, and 11% (1/9) of participants dropped out prior to baseline physical function testing because of feeling overwhelmed. Of the 6 palliative cancer patients who completed baseline physical function testing, 33% (2/6) of participants dropped out during Week One of the intervention program because of severe dyspnea and pain, and 17% (1/6) participants dropped out during Week Five of the intervention program because of terminal delirium. 50% (3/6) of the participants who completed baseline physical function testing, also completed the intervention program and post-intervention assessments.

Given that only 3 participants completed the intervention program and post-intervention assessments, inferential statistics were not possible and all accumulated data was reviewed descriptively. Hence the following 3 case reports are presented to review these participants who completed the program.

IV-4. CASE REPORTS

IV-4.1. Case #1

Diagnosis and Cancer Treatment

A 56 year-old man was diagnosed with cancer of unknown primary, with metastases of the lung, liver, bone and brain. He received a full course of palliative whole-brain radiotherapy (WBRT), and daily dexamethasone was initiated. He was recruited from the outpatient radiotherapy unit during his first week of WBRT. Clinician-estimated prognosis at the time of study recruitment was approximately 4 months or less.

Initial Assessment

Upon baseline assessment, the participant had a body mass index of 59.0 kg/m^2, and a palliative performance scale (PPS) level of 70%. The participant indicated that his physical limitations had the greatest negative effect on his quality of life over the past week. He identified bilateral lower leg lymphedema as his most troublesome symptom, which primarily limited his mobility. His most common reported physical activity over the past week was climbing stairs within his home, in order to access his bedroom and bathroom on the top floor. The participant described the personal meaning of physical activity to him as: "better quality of life, and with any luck, prolonging life".

On baseline physical function testing, the participant experienced localized bony pain, rated 3/10, over the right posterior ribs with extension of the right arm, and increasing intention tremor of the left hand with the arm curl and grip strength maneuvers. Both symptoms resolved at the end of the respective tests. The participant's main concern during the six-minute walk test was increasing dyspnea and bilateral leg fatigue, both rated at 4/10 post-testing.

Individualized Home-Based Functional Walking program

Based on the results of baseline assessment and physical function testing, a home-based functional walking program (Table IV-4) was tailored towards the participant's ability and safety. It was noted that there was no change in dexamethasone dose over the course of the 6-week program. The participant was prescribed a daily walking plan of 5 minutes per day at low to moderate intensity,

adding 5 minutes per week to progress up to a total of 30 minutes per day at the end of the six-week program.

For the anaerobic exercise sessions, the participant was started with a blue Thera-band® (resistance level: 7.5 pounds of pull required to elongate band length by 100%) for the seated chest press and seated rowing exercises, and blue Thera-band® hand exercisers (resistance level: 8 pounds of force at 50% compression) for the ball squeeze exercise. The participant started with the 10-pound neoprene dumbbell for the arm curl exercise, and the 5-pound wrist cuff weight for the tricep curl exercise. Given his bilateral lower leg edema, the knee flexion exercise was started using only his leg weight as resistance; over the six-week program, he was slowly progressed up to the 3-pound ankle cuff weight. All exercises were started at 1 set of 8 repetitions, slowly progressing up to 2 sets of 8 repetitions for most exercises at the end of the six-week program, according to the pre-established guidelines (see Table IV-2).

Beginning in Week Two, the participant's main concern was that of intermittent bony pain in the left hip, with increase in fatigue. Subsequently he was unable to progress beyond walking 10 minutes per day before experiencing severe pain and fatigue. Modifications were made to the anaerobic exercises, with adoption of seated positions where possible. The participant completed 16 out of the 18 prescribed anaerobic exercise sessions, missing two anaerobic exercise sessions during Week Four and Week Five due to severe fatigue. The participant experienced no adverse events over the course of the six-week program.

Outcome Measurements

A summary of outcome measures is provided on Table IV-4. The participant lost nearly 9 kilograms of body weight over the six-week period, and improvements were noted in both upper and lower body flexibility. At the post-intervention assessment, the participant's PPS level was 60%; he reported intermittent syncope and significant total fatigue which likely impacted his endurance and mobility. As monitored by the *activ*PAL™ accelerometer, the average number of steps taken over the baseline week was 3714, with an average estimated total energy expenditure of 29.1 MET·hours; post intervention, the average number of steps taken during Week Six was 1471, with an average estimated total energy expenditure of 28.3 MET·hours.

When comparing baseline to post-intervention, the participant did report improvement in the MQOL total score, however both the LLFDI total physical functioning score and the BFI total global fatigue score worsened. Overall, the participant expressed high satisfaction with the physical activity program and identified the one-on-one supervision of the anaerobic exercise sessions as among its top advantages. When asked about what program aspects were least enjoyed, the participant indicated his decline in overall condition despite participating in the physical activity program. In follow-up, the participant eventually died 77 days after completing the study, having being hospitalized for severe dyspnea.

IV-4.2. Case #2

Diagnosis and Cancer Treatment

A 51 year-old woman was diagnosed with lung cancer and brain metastases. She received a full course of palliative WBRT, and daily dexamethasone was initiated. She was recruited from the outpatient radiotherapy unit after completion of WBRT.

Clinician-estimated prognosis at the time of study recruitment was approximately 6 months or less.

Initial Assessment

Upon baseline assessment, the participant had a body mass index of 42.1 kg/m^2, and a palliative performance scale (PPS) level of 70%. The participant indicated that fatigue was her most troublesome symptom, which she rated at 4/10. Her most common reported physical activity over the past week was walking approximately 30 minutes per day, for three times per week. The participant described the personal meaning of physical activity to her as: "part of having a positive outlook, and hope that I can prolong my life".

On baseline physical function testing, the participant experienced localized bony pain, rated 2/10, over her left medial knee upon extension of the left leg on the chair sit-and-reach and 30 second chair stand tests. The pain resolved after completion of each test. During the 6-minute walk test, her maximum heart rate was 135 beats per minute, and her minimum oxygen saturation was 93% on room air. She denied any fatigue or dyspnea post-testing.

Individualized Home-Based Functional Walking Program

Based on the results of baseline assessment and physical function testing, a home-based functional walking program (see Table IV-1) was tailored towards the participant's ability and safety. It was noted that the participant was being slowly weaned off the dexamethasone over the course of the 6-week program. The participant was prescribed a daily walking plan of 10 minutes per day at low to moderate

intensity, adding 5 minutes per week to progress up to a total of 40 minutes per day at the end of the six-week program.

For the anaerobic exercise sessions, the participant was started with a blue Thera-band® (resistance level: 7.5 pounds of pull required to elongate band by 100%) for the seated chest press and seated rowing exercises, and black Thera-band® hand exercisers (resistance level: 17.0 pounds of force at 50% compression) for the ball squeeze exercise. The participant started with the 7-pound neoprene dumbbell for the arm curl exercise, and the 5-pound wrist cuff weight for the tricep curl exercise. During Week Two, the participant was switched to the green Thera-band® (resistance level: 5.0 pounds of pull required to elongate band by 100%) for the tricep curl exercise in order to better isolate and train the triceps bilaterally. Given her intermittent left medial knee pain, the knee flexion exercise was started using only her leg weight as resistance; over the six-week program, she was slowly progressed up to the 3-pound ankle cuff weight. All exercises were started at 1 set of 8 repetitions, slowly progressing up to 2 sets of 10 repetitions for most exercises at the end of the six-week program, according to the pre-established guidelines (Table IV-2).

Beginning in Week Two, the participant's main concern was that of intermittent right anterior chest pain on palpation, rated 1.5/10, with no radiation, no associated dyspnea, and no aggravating or alleviating factors; follow-up with the oncologist determined the likely etiology to be the increasing size of the primary lung tumor. No modifications were required to the anaerobic exercises, although after acquiring an upper respiratory tract infection in Week Three, her subsequent dyspnea and fatigue resulted in the delay in progression of her daily walking program to 20

minutes per day. The participant completed 17 out of the 18 prescribed anaerobic exercise sessions, missing one anaerobic exercise sessions during Week Three due to the severe upper respiratory tract infection. The participant experienced no adverse events over the course of the six-week program.

Outcome Measurements

A summary of outcome measures is provided on Table IV-5. The participant lost 2.4 kilograms of body weight over the six-week period, and improvements were noted in the 8-Foot up-and-go, 30 second chair stand and the 6-minute walk. At the post-intervention assessment, the participant's PPS level was 70%; she reported residual symptoms of an upper respiratory tract infection, but denied any dyspnea post-testing. As monitored by the *activ*PAL™ accelerometer, the average number of steps taken over the baseline week was 11,373, with an average estimated total energy expenditure of 33.3 MET·hours; post intervention, the average number of steps taken during Week Six was 10,868, with an average estimated total energy expenditure of 32.5 MET·hours.

When comparing baseline to post-intervention, the participant did report decreases in the MQOL total and the BFI total global fatigue scores, however the LLFDI total physical functioning score improved. Overall, the participant expressed high satisfaction with the physical activity program and identified the home-based location of the program as among its top advantages. When asked whether she would be comfortable doing the program on her own with the aid of a handbook or DVD, the participant indicated her preference for one-on-one training, stating "then they can watch and see if I'm going the exercises right". In follow-up at 30 days post-

intervention, the participant had continued her daily walking regimen on her treadmill at home, and was being considered for palliative chemotherapy.

IV-4.3. Case #3

Diagnosis and Cancer Treatment

A 57 year-old man with hepatitis B was diagnosed with hepatocellular carcinoma post-liver transplant with subsequent liver, lung and bone metastases. He received palliative radiotherapy to the right shoulder and thoracic spine for bony metastatic pain, and was initiated on Tylenol #3 as needed for analgesia. He was not a candidate for chemotherapy given his immunosuppressive regimen post-liver transplant. He was recruited from the Regional Palliative Home Care Program after completing palliative radiotherapy. Clinician-estimated prognosis at the time of study recruitment was approximately 12 months or less.

Initial Assessment

Upon baseline assessment, the participant had a body mass index of 23.7 kg/m^2, and a palliative performance scale (PPS) level of 70%. He reported fatigue as his most troublesome symptom, which was rated at 4/10. His most common reported physical activity over the past week was walking approximately 60 minutes per day, for three times per week. The participant described the personal meaning of physical activity to him as: "helping me to cope, and maintain my independence…it gives me confidence that at least today, I can try to live normally".

On baseline physical function testing, the participant exhibited weakness of his right shoulder and arm which he reported as having began post-radiotherapy; in addition to limited active and passive range of motion of the right shoulder, its

weakness was most pronounced for the arm curl and grip strength tests. During the 6-minute walk test, his maximum heart rate was 112 beats per minute, and his minimum oxygen saturation was 87% on room air. His oxygen saturation recovered to 97% on room air at the end of the 6-minute walk. He denied any fatigue or dyspnea post-testing.

Individualized Home-Based Functional Walking Program

Based on the results of baseline assessment and physical function testing, a home-based functional walking program (see Table IV-1) was tailored towards the participant's ability and safety. The participant was prescribed a daily walking plan of 15 minutes per day at low to moderate intensity, adding 5 minutes per week to progress up to a total of 45 minutes per day at the end of the six-week program.

For the anaerobic exercise sessions, the participant was started with a green Thera-band® (resistance level: 5.0 pounds of pull required to elongate band length by 100%) for the seated chest press and seated rowing exercises, and blue Thera-band® hand exercisers (resistance level: 8.0 pounds of force at 50% compression) for the ball squeeze exercise. Given his right shoulder and arm weakness, the participant started with the 6-pound neoprene dumbbell for the arm curl exercise, and the green Thera-band® for the tricep curl exercise in order to minimize strain. The knee flexion exercise was started using only his leg weight as resistance; over the six-week program, he was slowly progressed up to the 2.5-pound ankle cuff weight. All exercises were started at 1 set of 8 repetitions, slowly progressing up to 1sets of 12 repetitions for most exercises at the end of the six-week program, according to the pre-established guidelines (see Table IV-2).

Beginning in Week Three, the participant's main concern was that of intermittent pain on palpation over enlarging right supraclavicular lymphadenopathy and left midaxillary lymphadenopathy, both rated 4/10; he was rotated to oral morphine for analgesia, and had single fraction palliative radiotherapy to both the right neck and left axilla during Week Four. The participant reported worsening nausea post-palliative radiotherapy, with a maximum rating of 5/10, and subsequently progression in the number of sets/repetitions in the anaerobic exercises and the daily walking prescription was delayed. During Week Four, the participant also exhibited increasing difficulties with balance due to intermittent syncope, and anaerobic exercises were performed in the seated position where possible. The participant completed 14 out of the 18 prescribed anaerobic exercise sessions, missing one session during Week Four due to palliative radiotherapy, and missing three non-consecutive sessions during Weeks Five and Six due to severe nausea.

Outcome Measurements

A summary of outcome measures is provided on Table IV-6. The participant gained 1.0 kilogram of body weight over the six-week period, and an overall decline was noted in the objective physical function tests. At the post-intervention assessment, the participant's PPS level was 60%; he reported significant nausea and fatigue, neither of which worsened post-testing. As monitored by the *activ*PAL™ accelerometer, the average number of steps taken over the baseline week was 7,232, with an average estimated total energy expenditure of 29.1 MET·hours; post intervention, the average number of steps taken during Week Six was 1,159, with an average estimated total energy expenditure of 26.9 MET·hours.

When comparing baseline to post-intervention, the participant did report improvement in the MQOL total score, however there was a decline in both the LLFDI total physical functioning and the BFI total global fatigue scores. Overall, the participant expressed high satisfaction with the physical activity program and identified the anaerobic component of the program as among its top advantages. When asked about any negative experiences with the physical activity program, the participant indicated his inability to sustain the aerobic walking component on his own given his increased symptom burden post-radiotherapy. In follow-up at 30 days post-intervention, the participant's medical condition had declined such that he was spending the majority of the day sitting or supine.

IV.5. DISCUSSION

The purposes of this study were to examine the initial development and pilot-testing of a physical activity program, and to assess the preliminary effects of this intervention on supportive care outcomes in palliative cancer patients. Based on our preliminary survey data, a significant majority of the palliative cancer sample indicated a preference for a home-based physical activity program, with walking and resistance training being the top two endorsed modalities of physical activity (unpublished data). With the aim of optimizing adherence rates and supportive care outcomes, therefore, a modified home-based functional walking program was designed to incorporate the specific physical activity programming interests and preferences of this population.

There are a number of feasibility issues deserving of attention from this study. From our pilot survey study, we were able to recruit 50 palliative cancer patients over

a 7 month period (unpublished data); using the same eligibility criteria and local recruitment strategy, however, we were only able to recruit 9 palliative cancer patients over a 6 month period. A total of 504 patients were screened through the Regional Palliative Home Care and Cross Cancer Institute outpatient radiotherapy units on behalf of all palliative care research studies that were open for accrual during that 6-month period, however only 15% (76/504) consented to being contacted with regards to this particular study. In both Regional Palliative Home Care and Cross Cancer Institute outpatient radiotherapy units, the local recruitment strategy does not consistently define clinician-estimated life expectancy within 3 to 12 months for every screened patient, so we are unable to determine the true proportion of patients who fulfilled all eligibility criteria for this study at the time of initial screening. As such, tracking of all eligibility criteria for this study, including clinician-estimated life expectancy within 3 to 12 months, could occur only on patients who consented to be contacted by the study coordinator.

Of the 96 patients who consented to being contacted by the study coordinator, 53% (51/96) fulfilled all eligibility criteria for this study. Therefore of all patients who consented to being contacted by the study coordinator and who met all eligibility criteria for this study, our accrual rate was 18% (9/51). Locally, this accrual rate is comparable to Hutton et al.'s study (2006) of dietary intake in 151 advanced cancer patients, wherein the authors reported an estimated 21% accrual rate from both the Cross Cancer Institute and Regional Palliative Home Care (41). On a larger scale, Abernethy et al. (2006) conducted a 2 x 2 x 2 factorial cluster RCT examining an educational intervention in 461 palliative care patients and their general practitioners,

and reported an eligibility rate of 31%, with subsequent randomization of 76% of the eligible cohort (42); their estimated accrual rate of 24% has been shown to be fairly typical of large palliative care trials (43), and is slightly higher than that of our study.

In comparison to other feasibility studies of physical activity interventions in palliative cancer patients, Porock et al. (2000) reported a recruitment rate of 46% (11/24) in their pilot study of 4-week home-based exercise program in home hospice care patients, with incomplete information as to attrition rates and reasons for withdrawal (15). Of the 63 palliative cancer patients who agreed to participate in the 6-week group exercise program in Oldervoll et al.'s pilot study (2005), a recruitment rate of 62% (63/101) and an attrition rate of 46% (29/63) was reported; the most frequent reasons for withdrawal was considerable disease progression and pain (14). Given that the median survival of our pilot survey population was 104 days, and the recruitment procedure for this study was similar to that of the pilot survey, it is likely that our participants were further along on the cancer trajectory. In light of the progression in tumor and symptom burden in palliative cancer patients, untimely attrition over a 6-week period in this population with such limited prognosis is not unexpected (44).

From our pilot survey study, an overwhelming majority of respondents indicated that they were interested in and able to participate in a physical activity program. The ability to participate in a physical activity program, however, may fluctuate on a day-to-day basis depending on patient-reported symptoms: 69% (35/51) of eligible patients declined consent to the study because of severe symptoms at the time of initial assessment, with fatigue being the most common reported symptom. In

a prospective study of 400 palliative home care patients with a mean survival of 52 days, Mercadante et al. (2000) reported an increase in dyspnea and fatigue scores over time, with a peak in symptom intensity and frequency at the lowest levels of Karnofsky performance status (45); these findings suggest a progressive correlation between physical functioning and symptom prevalence over time. Therefore, over the 6-week duration of our intervention program, the maintenance of symptom stability or even the slowing of physical functional decline may be realistic goals for this palliative cancer population.

Of the 9 palliative cancer patients who enrolled in our study, 67% (6/9) dropped out with the most common reason being admission to acute care for severe symptoms. This rate of attrition is higher when compared to large palliative care trials; in a multicenter RCT examining the effects of oral cannabinoids on appetite and quality of life in 243 advanced cancer patients, Strasser et al. (2006) reported a dropout rate of 33% (79/243) over the course of their 6-week long intervention (46). The authors reported that the most common reason for dropout was "withdrawn consent", with 59% (47/79) of dropouts occurring within 4 weeks of starting this pharmacological intervention (46). In contrast, 83% (5/6) of dropouts occurred within 4 weeks of starting our physical activity intervention. Although each of our three case reports indicated that the 6-week program duration was acceptable, shortening the duration of intervention may be a potential next step for future feasibility trials.

Despite increasing symptom burdens over the course of the study, all three participants were able to complete all six weeks of the intervention program, with adherence rates for the prescribed anaerobic exercise sessions ranging from 78% to

94%. Moreover, in all three cases presented, there were no reported adverse effects from the prescribed intervention. Overall, all three participants reported high satisfaction with this physical activity program, indicating that the home-based location, one-on-one supervision, and anaerobic exercise sessions were primary advantages.

As there were individual differences in symptom burdens and physical functioning between the three cases, the modified home-based functional walking program was individualized to each participant with the goal of maximizing safety and tolerability. The aerobic prescription of daily walking was tailored to the participant's previous reported physical activity behavior and their performance on the baseline 6-minute walk test; likewise, the prescription of anaerobic exercises took into consideration any physical impairments identified on initial assessment, as well as the participant's performance on baseline physical function testing. All exercises started at low resistance and progressed within the participant's tolerance over a 6-week period, which allowed for adequate time to observe for potential physical responses.

In two of the three cases presented, improvements were noted in total MQOL scores. In contrast, two of the three cases showed a decline in total physical functioning, as demonstrated by the total LLFDI scores. All three participants shared an overall trend towards worsening ESAS symptom scores, and worsening total BFI global fatigue scores, post-intervention. In general, there were no significant changes in HDS scores for any participant after completion of the physical activity program. Because of our case study design, it is not possible to distinguish whether these effects were secondary to the physical activity program or to progression in the underlying

cancer; as shown in Headley et al.'s pilot RCT (2004) of a seated exercise program in stage IV breast cancer patients (47), a slowing of the inevitable decline in fatigue and quality of life scores may be the realistic interventional goal which would account for the changes seen in our case series.

Interestingly, the participant in case #2 reported both an improvement in the ESAS fatigue score and a decline in the BFI total global fatigue score; this highlights the difference between using a single-item measure and a multidimensional tool for assessment of cancer-related fatigue (48). In addition, case #2 was the only participant who showed an improvement in total LLFDI scores, in particular the LLFDI basic lower extremity functioning score; at the same time, case #2 was being tapered off dexamethasone therapy during the course of the study. Case #1, on the other hand, reported a worsening in total LLFDI scores post-intervention, and was taking the same dexamethasone dose throughout the 6-week intervention. One of the most prominent adverse effects of steroids is proximal myopathy (49); although our case study design precludes being able to determine causality, the potential link between lower body physical function and steroid therapy is suggestive.

In all three cases, increasing symptom burden over the course of the 6-week program resulted in the delay in progression in both the aerobic and anaerobic components of the modified home-based functional walking program. As evident from the *activ*PAL™ data, the number of steps and the estimated total energy expenditure decreased significantly over the course of 6-weeks. Although none of the three participants achieved the target daily walking prescription at the end of the 6-week program, all 3 participants were able to continue both aerobic and anaerobic

components at reduced levels. Currently, there is no recommended minimum level of physical activity for palliative cancer patients, however any amount of physical activity that the patient can tolerate would appear to be better than engaging in no activity at all. Hence one-on-one supervision takes on greater significance in our study, wherein modifications could be made to anaerobic exercises without missing the entire session completely.

On the other hand, one-on-one supervision of thrice weekly anaerobic sessions in the patient's home, resulted in the inevitable exclusion of potentially eligible participants. Of the 20 eligible patients who were screened from the Department of Symptom Control and Palliative Care and the Cross Cancer Institute outpatient radiotherapy units and who consented to being contacted by the study coordinator, 35% (7/20) were unable to participate because they lived out-of-town. While having one-on-one supervision was identified as one of the top advantages by the three presented case reports, the option of a self-directed intervention by means of an instructional handbook or video may increase accrual in future pilot trials.

Our case series provides data from which future feasibility studies can be launched. With respect to the local recruitment strategy in both Regional Palliative Home Care and the Cross Cancer Institute outpatient radiotherapy units, further medical and demographic characterization of the patient population at the time of initial screening, including exploration of the reasons for declining consent to be contacted for research, would aid in defining which subgroup of the palliative cancer population would most benefit from a physical activity intervention, in addition to enhancing eligibility and accrual rates. Further modifications of the home-based

functional walking program, such as shortening the duration of the intervention, examining the effects of aerobic or anaerobic components separately, and including an option for self-directed physical activity programming, may also optimize recruitment and retention.

In summary, our case series demonstrates the feasibility of certain elements of a modified home-based functional walking program in a limited number of palliative cancer patients. In all three cases presented, participants were able to complete a 6-week long physical activity intervention with no adverse events; two of the three cases presented showed an improvement in overall QoL scores post-intervention with very high adherence rates. Moreover, all three participants expressed high satisfaction with the modified home-based functional walking program, particularly with respect to the home-based location, individual supervision and inclusion of anaerobic exercise sessions. Clearly these case studies provide further rationale for additional pilot and feasibility research on a physical activity intervention in palliative cancer patients.

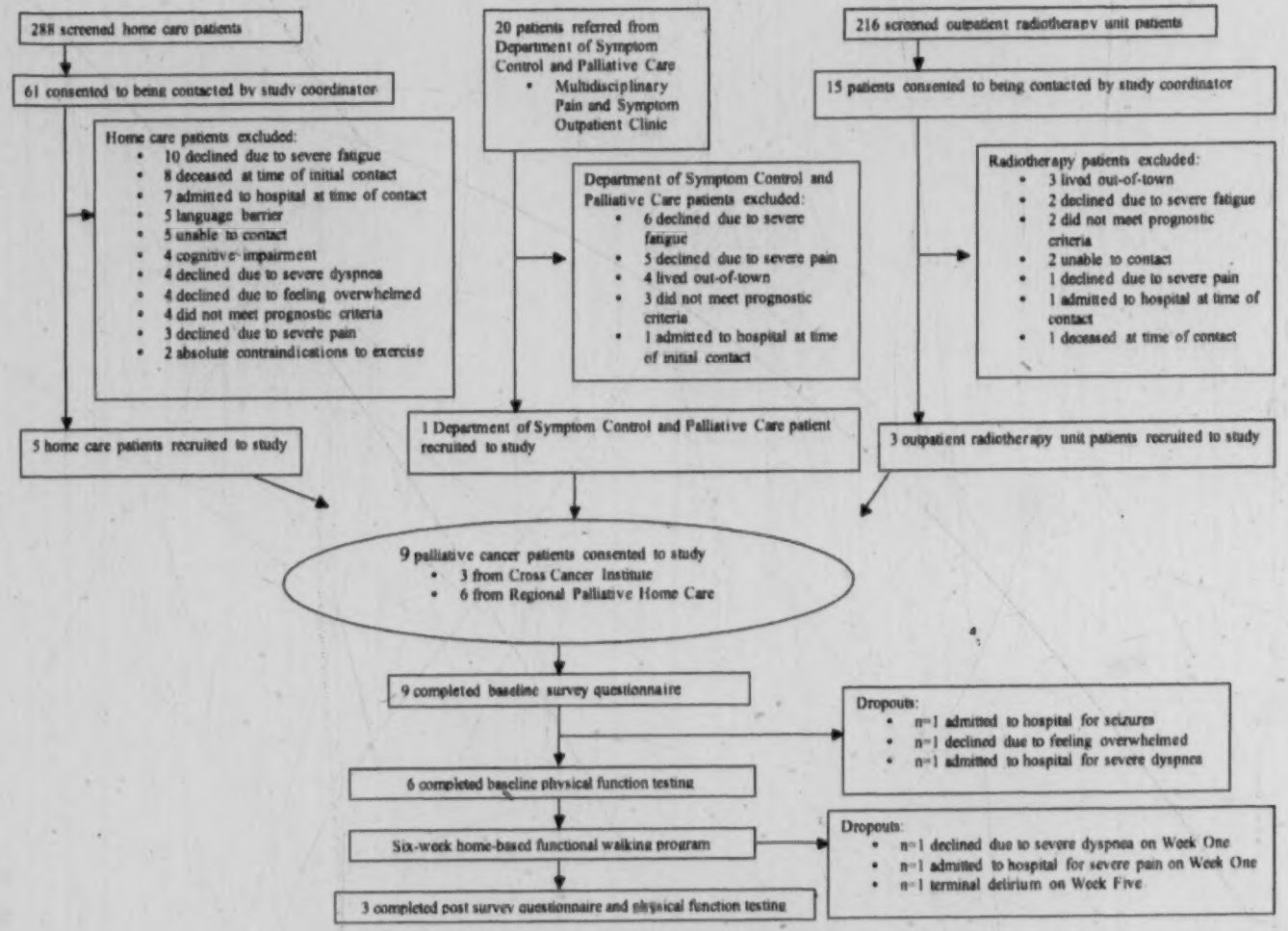
288 screened home care patients
61 consented to being contacted by study coordinator
Home care patients excluded:
• 10 declined due to severe fatigue
• 8 deceased at time of initial contact
• 7 admitted to hospital at time of contact
• 5 language barrier
• 5 unable to contact
• 4 cognitive impairment
• 4 declined due to severe dyspnea
• 4 declined due to feeling overwhelmed
• 4 did not meet prognostic criteria
• 3 declined due to severe pain
• 2 absolute contraindications to exercise
5 home care patients recruited to study
20 patients referred from Department of Symptom Control and Palliative Care
• Multidisciplinary Pain and Symptom Outpatient Clinic
Department of Symptom Control and Palliative Care patients excluded:
• 6 declined due to severe fatigue
• 5 declined due to severe pain
• 4 lived out-of-town
• 3 did not meet prognostic criteria
• 1 admitted to hospital at time of initial contact
1 Department of Symptom Control and Palliative Care patient recruited to study
216 screened outpatient radiotherapy unit patients
15 patients consented to being contacted by study coordinator
Radiotherapy patients excluded:
• 3 lived out-of-town
• 2 declined due to severe fatigue
• 2 did not meet prognostic criteria
• 2 unable to contact
• 1 declined due to severe pain
• 1 admitted to hospital at time of contact
• 1 deceased at time of contact
3 outpatient radiotherapy unit patients recruited to study
9 palliative cancer patients consented to study
• 3 from Cross Cancer Institute
• 6 from Regional Palliative Home Care
9 completed baseline survey questionnaire
Dropouts:
• n=1 admitted to hospital for seizures
• n=1 declined due to feeling overwhelmed
• n=1 admitted to hospital for severe dyspnea
6 completed baseline physical function testing
Six-week home-based functional walking program
Dropouts:
• n=1 declined due to severe dyspnea on Week One
• n=1 admitted to hospital for severe pain on Week One
• n=1 terminal delirium on Week Five
3 completed post survey questionnaire and physical function testing

Figure IV-1. Flow of Participants through the Study

Table IV-1: Modified home-based functional walking (FW) program: Warm-up exercises

Warm-up exercise	Purpose	Target muscle / joint	Examples of equipment	Position
1. Chin to Chest	Range of motion	Cervical spine	None	Seated
2. Chin to Shoulder	Range of motion	Cervical spine	None	Seated
3. Shoulder Shrugs	Range of motion	Shoulder joint	None	Seated
4. Arm Swing	Range of motion	Shoulder joint	None	Seated
5. Rowing	Range of motion	Shoulder and elbow joints	None	Seated
6. Forward hugs	Range of motion	Lower back and upper arms	None	Seated
7. Up and down leg march	Range of motion	Hip joint	None	Seated or Standing
8. Out and in leg march	Range of motion	Hip joint	None	Seated or Standing
9. Foot forward and backward	Range of motion	Knee joint	None	Seated or Standing
10. Toe point/flex and Wrist flex/extend	Range of motion	Ankle and wrist joints	None	Seated

Table IV-1 continued: Modified home-based functional walking (FW) program: Muscle strengthening and Balance retraining

Exercise	Purpose	Target muscle / joint	Examples of equipment	Position
11. Ball squeeze	Resistance training Grip strength	Wrist and forearm muscles	Thera-band® hand exercisers	Seated
12. Chest press	Resistance training	Pectoralis major, triceps and deltoids	Thera-bands®	Seated
13. Rowing	Resistance training	Latissimus dorsi, trapezius, biceps and deltoids	Thera-bands®	Seated
14. Biceps curl	Resistance training	Biceps	Neoprene dumbbells	Seated
15. Triceps curl	Resistance training	Triceps	Thera-bands® or neoprene dumbbells	Seated
16. Sit to stand	Resistance training	Quadriceps, hamstrings and gluteals	None	Seated and Standing
17. Knee flexion	Resistance training	Hamstrings	Ankle cuff weights	Seated or Standing
18. Toe raises	Balance retraining	Tibialis anterior	None	Standing
19. Heel raises	Balance retraining	Gastrocnemius and soleus	None	Standing

Table IV-1 continued: Modified home-based functional walking (FW) program: Cool-down exercises

Cool-down exercise	Purpose	Target muscle / joint	Examples of equipment	Position
20. Swan	Stretching	Pectoralis major, deltoids and biceps	None	Seated
21. Zipper stretch	Stretching Flexibility	Latissimus dorsi and triceps	Thera-bands®	Seated or Standing
22. Tibia touch	Stretching Flexibility	Hamstrings and spinal erectors	None	Seated
23. Outer thigh stretch	Stretching	Hip abductors	None	Seated
24. Quadriceps stretch	Stretching	Quadriceps and tibialis anterior	None	Seated or Standing
25. Calf stretch	Stretching	Gastrocnemius and soleus	None	Seated or Standing

Table IV-2: Guidelines for the modified home-based functional walking (FW) program

Program components	General guidelines
1. Muscle strengthening	Whole body resistance training with special emphasis on lower body muscle strengthening for transferring, standing, walking and prevention of falls
	Balanced resistance training of opposing muscle groups: Chest/back muscles Biceps/triceps Quadriceps/hamstrings Tibialis anterior/gastrocnemius and soleus
	Maintenance of proper technique, breathing and positioning on range of motion prior to use of resistance equipment
2. Balance retraining	Whole body balance training with special emphasis on ankle dorsiflexors and plantarflexors for recovery of balance
	Maintenance of posture and balance using body weight alone prior to adding resistance equipment
3. Intensity	Goal of low to moderate intensity measured using Borg's ratings of perceived exertion (RPE) (0-10)

Table IV-2 continued: Guidelines for the modified home-based functional walking (FW) program

Program components	General guidelines
4. Resistance	Progression by: • Supported to unsupported positions • Range of motion or body weight to addition of resistance equipment • Start with the lightest resistance equipment and upwards • Increasing number of sets/repetitions prior to progression of resistance level Reduce workload if: • Increased pain, fatigue or shortness of breath post exercise • Muscle pain or soreness > 48 hours Terminate session if: • Excessive pain, fatigue or shortness of breath post exercise
5. Sets	Progression by: • Start with one set of 8 repetitions per exercise • RPE ≤ 3 consistent for ≥ 2 sessions prior to increasing number of repetitions by 2 until maximum of 15 repetitions per set • Once one set of 15 repetitions achieved, advanced to two sets of 8 repetitions
6. Frequency	3 days per week, on non-consecutive days

Table IV-3: Objective Physical Function Measures (listed in the order of testing)

Physical Function Test	Purpose	General description
1. 8-Foot up-and-go	Agility and dynamic balance	Number of seconds required to get up from a seated position, walk 8 feet, turn and return to a seated position
2. Chair sit-and-reach	Lower body flexibility	Number of centimeters between extended fingers and tip of toe, when leg extended and hands reaching towards toes from a seated position at the front of a chair
3. Arm curl	Upper body strength	Number of bicep curls completed in 30 seconds holding a hand weight (5 lbs for women, 8 lbs for men)
4. Back scratch	Upper body flexibility	Number of centimeters between extended middle fingers, when one hand is reaching over the shoulder and the opposite hand up the middle of the back
5. Grip strength	Hand and forearm strength	Number of kilogram·feet measured on handheld dynamometer (average of 2 measurements per side)
6. 30 second chair stand	Lower body strength	Number of full stands completed in 30 seconds from a seated position

Table IV-3 continued: Objective Physical Function Measures (listed in the order of testing)

Physical Function Test	Purpose	General description
7. Four test balance scale	Static balance	Number of seconds up to 10 seconds each that participant is able to sustain 1) feet together stand, 2)semi-tandem stand, 3) tandem stand and 4) one leg stand
8. 6-minute walk	Aerobic endurance	Number of meters that participant can walk in 6 minutes around a 45.7 meter course

Table IV-4: Outcome Measures for participant presented in Case #1

Outcome Measure	Assessment	Baseline	Post Six-Week Intervention
1. MQOL	Physical Symptoms (0-10)	6.0	5.5
	Physical Well-Being (0-10)	7.0	6.0
	Psychological (0-10)	10.0	10.0
	Existential (0-10)	9.6	9.7
	Support (0-10)	10.0	10.0
	TOTAL SCORE (0-10)	8.5	8.2
2. LLFDI	Upper Extremity Functioning (0-25)	0	9.0
	Basic Lower Extremity Functioning (0-25)	3.0	6.0
	Advanced Lower Extremity Functioning (0-25)	9.0	17.0
	TOTAL SCORE (0-75)	12.0	32.0
3. ESAS	Pain (0-10)	2.0	2.0
	Fatigue (0-10)	4.0	3.0
	Nausea (0-10)	0.5	0
	Depression (0-10)	0	0
	Anxiety (0-10)	0	0
	Drowsiness (0-10)	0	0
	Appetite (0-10)	0	5.0
	Well-Being (0-10)	0	3.0
	Dyspnea (0-10)	0	0
4. BFI	TOTAL Global Fatigue (0-10)	2.0	4.8
5. HDS	Authentic Spirit Factor (1-7)	1.0	1.0
	Comfort Factor (1-7)	3.3	3.3

Table IV-4 continued: Outcome Measures for participant presented in Case #1

Outcome Measure	Assessment	Baseline	Post Six-Week Intervention
6. Physical Parameters	Height (m)	1.6	1.6
	Weight (kg)	158.8	150.1
	BMI (kg/m^2)	59.0	55.8
	Resting Blood Pressure (mm Hg)	138/80	112/72
	Resting Heart Rate (bpm)	86	83
7. 8-Foot up-and-go	Number of seconds required	12.4	14.0
8. Chair sit-and-reach	Left (number of centimeters)	-30.0	-15.0
	Right (number of centimeters)	-33.0	-15.0
9. Arm curl	Left (number of repetitions)	15	12
	Right (number of repetitions)	16	12
10. Back scratch	Left (number of centimeters)	-24.0	-31.0
	Right (number of centimeters)	-32.0	-29.0
11. Grip strength	Left (kg·feet)	32.0	34.0
	Right (kg·feet)	31.8	31.8
12. 30 second chair stand	Number of repetitions	10	8
13. Four test balance scale	Feet together (number of seconds)	10.0	10.0
	Semi-tandem (number of seconds)	10.0	10.0
	Tandem (number of seconds)	10.0	0
	One leg stand (number of seconds)	2.81	0
14. 6-minute walk	Total distance (m)	264.0	162.4

Table IV-5: Outcome Measures for participant presented in Case #2

Outcome Measure	Assessment	Baseline	Post Six-Week Intervention
1. MQOL	Physical Symptoms (0-10)	7.2	8.3
	Physical Well-Being (0-10)	9.0	9.0
	Psychological (0-10)	9.4	9.3
	Existential (0-10)	10.0	10.0
	Support (0-10)	10.0	10.0
	TOTAL SCORE (0-10)	9.1	9.3
2. LLFDI	Upper Extremity Functioning (0-25)	5.0	0
	Basic Lower Extremity Functioning (0-25)	6.5	0
	Advanced Lower Extremity Functioning (0-25)	5.0	5.0
	TOTAL SCORE (0-75)	16.5	5.0
3. ESAS	Pain (0-10)	0	1.0
	Fatigue (0-10)	4.0	3.0
	Nausea (0-10)	0	4.0
	Depression (0-10)	0	0
	Anxiety (0-10)	0	2.5
	Drowsiness (0-10)	0	0
	Appetite (0-10)	0	3.0
	Well-Being (0-10)	0	2.0
	Dyspnea (0-10)	0	0
4. BFI	TOTAL Global Fatigue (0-10)	0.1	2.3
5. HDS	Authentic Spirit Factor (1-7)	1.0	1.0
	Comfort Factor (1-7)	2.5	3.3

Table IV-5 continued: Outcome Measures for participant presented in Case #2

Outcome Measure	Assessment	Baseline	Post Six-Week Intervention
6. Physical Parameters	Height (m)	1.6	1.6
	Weight (kg)	84.9	82.5
	BMI (kg/m^2)	34.0	33.0
	Resting Blood Pressure (mm Hg)	122/76	106/80
	Resting Heart Rate (bpm)	93	88
7. 8-Foot up-and-go	Number of seconds required	5.81	5.44
8. Chair sit-and-reach	Left (number of centimeters)	+1.0	+1.0
	Right (number of centimeters)	+2.0	+2.0
9. Arm curl	Left (number of repetitions)	15	15
	Right (number of repetitions)	13	17
10. Back scratch	Left (number of centimeters)	+2.0	+0.5
	Right (number of centimeters)	+3.0	+2.0
11. Grip strength	Left (kg·feet)	24.3	24.5
	Right (kg·feet)	32.0	31.0
12. 30 second chair stand	Number of repetitions	13	17
13. Four test balance scale	Feet together (number of seconds)	10.0	10.0
	Semi-tandem (number of seconds)	10.0	10.0
	Tandem (number of seconds)	10.0	10.0
	One leg stand (number of seconds)	10.0	10.0
14. 6-minute walk	Total distance (m)	467.4	488.7

Table IV-6: Outcome Measures for participant presented in Case #3

Outcome Measure	Assessment	Baseline	Post Six-Week Intervention
1. MQOL	Physical Symptoms (0-10)	7.0	5.0
	Physical Well-Being (0-10)	5.0	4.0
	Psychological (0-10)	10.0	9.5
	Existential (0-10)	9.3	6.7
	Support (0-10)	8.5	9.0
	TOTAL SCORE (0-10)	8.0	6.8
2. LLFDI	Upper Extremity Functioning (0-25)	14.0	20.0
	Basic Lower Extremity Functioning (0-25)	5.0	14.0
	Advanced Lower Extremity Functioning (0-25)	8.0	21.0
	TOTAL SCORE (0-75)	27.0	55.0
3. ESAS	Pain (0-10)	3.0	4.0
	Fatigue (0-10)	4.0	7.0
	Nausea (0-10)	0	7.0
	Depression (0-10)	0	0
	Anxiety (0-10)	0	0
	Drowsiness (0-10)	1.0	6.0
	Appetite (0-10)	1.0	10.0
	Well-Being (0-10)	2.0	4.0
	Dyspnea (0-10)	1.0	3.0
4. BFI	TOTAL Global Fatigue (0-10)	2.0	6.9
5. HDS	Authentic Spirit Factor (1-7)	1.2	2.0
	Comfort Factor (1-7)	2.0	3.5

Table IV-6 continued: Outcome Measures for participant presented in Case #3

Outcome Measure	Assessment	Baseline	Post Six-Week Intervention
6. Physical Parameters	Height (m)	1.6	1.6
	Weight (kg)	59.1	60.1
	BMI (kg/m^2)	23.7	24.1
	Resting Blood Pressure (mm Hg)	148/80	132/90
	Resting Heart Rate (bpm)	84	108
7. 8-Foot up-and-go	Number of seconds required	8.41	10.00
8. Chair sit-and-reach	Left (number of centimeters)	0	-12.0
	Right (number of centimeters)	0	-11.0
9. Arm curl	Left (number of repetitions)	18	11
	Right (number of repetitions)	14	10
10. Back scratch	Left (number of centimeters)	-27.0	-30.0
	Right (number of centimeters)	-24.5	-24.0
11. Grip strength	Left (kg·feet)	34.0	25.5
	Right (kg·feet)	16.0	17.0
12. 30 second chair stand	Number of repetitions	15	11
13. Four test balance scale	Feet together (number of seconds)	10.0	10.0
	Semi-tandem (number of seconds)	10.0	10.0
	Tandem (number of seconds)	10.0	2.0
	One leg stand (number of seconds)	4.0	0
14. 6-minute walk	Total distance (m)	320.0	250.9

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V. CHAPTER FIVE

DISCUSSION

V-1. DISCUSSION

The purpose of this thesis was to examine the role of physical activity as a supportive care intervention in palliative cancer patients. As shown by the systematic review, there is a paucity of research on physical activity interventions in this population. Our studies add to the growing body of feasibility research on physical activity within palliative cancer populations, by demonstrating that limited numbers of these patients are able to participate in physical activity interventions with indications of positive effects on supportive care outcomes. The predominance of pilot studies precludes the ability to make clinically meaningful recommendations about what type or how much physical activity would be most beneficial for palliative cancer patients. The current state of evidence is insufficient to draw conclusions about the efficacy of physical activity as a supportive care intervention in this population.

As shown by the pilot survey, the majority of palliative cancer patients in our sample felt willing and able to participate in a physical activity intervention, with a strong preference for home-based programs. Walking was reported as the most common physical activity over the past week, as well as the most preferred modality for physical activity. Furthermore, those respondents who reported higher walking and total physical activity levels over the past week, had a strong association with higher quality of life scores. This strong interest in physical activity and identification of specific preferences formed the basis upon which a modified home-based functional walking program was developed for palliative cancer patients. Our case series highlights that a limited number of palliative cancer patients are able to tolerate and

complete a home-based physical activity intervention, with at least some of these patients reporting improvements in supportive care outcomes post-intervention.

Taken together, these findings suggest that further feasibility studies are required in order to advance this field of research. From these preliminary studies, there is no compelling reason to discourage physical activity to palliative cancer patients, in that it appears to pose no greater risk of harm; however, there is insufficient data from which to definitively endorse physical activity interventions in this population.

V-1.1: Systematic Review

Currently, ours is the first systematic review of the best available evidence of physical activity as a supportive care intervention in palliative cancer patients. The initial screen of 14 electronic databases, handsearching of 3 major palliative care journals and 2 major palliative care conference proceedings, including reference lists, yielded 6036 studies, which attests to the comprehensiveness of the search strategy. Moreover, field experts were contacted to identify unpublished studies, and non-English language articles were translated, thus increasing the potential yield of studies. Study selection, data abstraction and quality assessment were performed independently by two reviewers, thus enhancing the rigor of the review.

An additional strength of the systematic review is the search of grey literature through specialized electronic databases such as Proquest Theses & Dissertations. By including research that has not been formally published in peer-reviewed literature, the effect of publication bias is minimized and subsequently the thoroughness of the systematic review is enhanced [1]. Cook et al. (2001) conducted a systematic review

into the efficacy of palliative care teams, with inclusion of the System for Information on Grey Literature (SIGLE) database as part of their search strategy; the authors concluded that the efficiency of grey literature searching in palliative care may be low, due to the variable quality of indexing of evaluative research in palliative care [2]. However, given that the aim of our review was not to evaluate efficacy, but rather to describe the best available evidence, the inclusion of grey literature searching did aid in identifying potentially relevant studies in this emerging area of research in physical activity interventions in palliative cancer patients.

By narrowing our systematic review inclusion criteria to studies of cancer patients with a clinician-estimated prognosis of 12 months or less, our overall yield of included studies was restricted: 5% (7/154) of potentially relevant studies were excluded based on this criterion. The majority of excluded studies did not report on participant life expectancy or actual survival, therefore the reviewers estimated life expectancy of the participants based on the reported medical data. Prognostication by clinicians, however, has been found to be inaccurate, and current tools for survival prediction require further refinement and validation in the terminally ill [3].

Another limitation of the systematic review was the *a priori* decision to exclude studies that involved a mixed population of different stages of disease, if they did not report data or analyze data separately by disease stage. 6% (9/154) of potentially relevant studies were excluded based on this decision; nearly all of these studies reported the number of participants in each stage I to IV, but the outcome data was presented cumulatively for the entire cohort. In addition, this *a priori* decision was confounded by the fact that depending on the specific cancer diagnosis, stage IV

disease could still fall outside a clinician-estimated life expectancy of less than 12 months: for example, stage IV testicular cancer would not meet our prognostic criteria. This decision may have restricted our yield of included studies and hence impacted the overall quality of the review.

V-1.2: Pilot Survey

Currently, ours is the first study to examine the specific interests and preferences for physical activity in palliative cancer patients. In addition, ours is the first study to explore potential associations between patient-reported physical activity and quality of life outcomes in palliative cancer patients with tracking of actual survival from time of survey to time of death. Additional study strengths include the use of the MQOL and ESAS tools, both of which have been widely tested and validated in palliative cancer populations [4, 5].

In a survey of 128 advanced cancer patients who had an estimated life expectancy of between 6 months and 5 years and who were all actively receiving chemotherapy, Clark et al. (2007) showed that participants reported engaging in one bout of moderate exercise per week and three bouts of mild exercise per week, on average, using the Godin Leisure-Time Exercise Questionnaire (GLTEQ) [6]. Exercise is defined as any form of physical activity which an individual undertakes during leisure time and that is done repeatedly over an extended time period with the goal of improving fitness or health [7]; according to the GLTEQ, participants are asked to recall their average weekly exercise divided into strong, moderate and mild intensity categories, relative to its effect on the participant's heart rate and perspiration [8]. Assuming that each bout of exercise is 15 minutes or longer in duration, Clark et al.

(2007) reported that their average total participant-reported exercise would be of at least mild intensity, for a minimum of 1 hour per week [6].

As opposed to the estimated life expectancy of between 6 months and 5 years in Clark et al.'s (2007) sample [6], our participants showed a median actual survival of 104 days from time of survey to time of death; although Clark et al. (2007) did not report on the performance status of their participants, it is likely that our sample was much further along the cancer trajectory, and thus their tumor and symptom burdens were likely substantially greater. Autonomic dysfunction becomes more prevalent at the end stages of cancer, with fixed heart rates and variable sweating being common clinical manifestations [9]; using these parameters as measures of exercise intensity in the GLTEQ, therefore, may be potentially confounding in palliative cancer patients. In addition, none of our participants reported engaging in physical activities that would meet the GLTEQ criteria for strenuous exercise (i.e. running, aerobics classes, cross country skiing, vigorous swimming or vigorous bicycling); the majority of our participants reported basic non-leisure time activities such as housework and climbing house stairs, as their common physical activities over the past week.

One potential limitation was the selection of inclusion criteria for study participants. For the purposes of all three studies, the inclusion criteria was defined as any patient with progressive, incurable, and locally recurrent or metastatic cancer, and a clinician-estimated life expectancy of less than 12 months. Defining a "palliative" population has been identified as one of the top methodological challenges of conducting palliative care research [10]; with respect to cancer, there is no standardized definition of a palliative patient, and multiple terms such as "advanced

cancer", "end-stage cancer" and "terminal cancer" have been used without uniform consensus as to the description of the eligible population [11]. In their survey study of Dutch general practitioners, Borgsteede et al. (2006) demonstrated significant differences in the elicited patient populations based on the different inclusion criteria of "non-curative treatment", "palliative care" and "death was expected"; the authors recommended that future research should include a combination of different criteria, including the intent of the palliative care provided as well as an assessment of the participant's life expectancy as an indicator of their chronological status along the cancer trajectory [11].

V-1.3: Case Series

Ours is the first physical activity intervention in palliative cancer patients that was designed and developed using their previously identified interests and preferences. The combination of patient-reported and objective measures of physical activity behavior, using the *activ*PAL™ accelerometer, also lends strength to the case series. The implementation of consistent one-on-one supervision of anaerobic exercise sessions, standardized set of basic anaerobic exercises and tailoring of programs to baseline physical functioning, maximized safety throughout the 6 weeks of the physical activity program. Initial development of this program under these rigorous conditions is crucial in order to establish feasibility before launching a larger pilot trial.

The selection of participant inclusion criteria likely influenced the low recruitment and retention rates for the case series. As evident by the flow of participants through the case series, the majority of screened patients who consented to

being contacted by the study coordinator were excluded due to severe symptoms or becoming deceased prior to initial contact (see Figure IV-1); these reasons for exclusion are among the most common practical challenges for recruitment in palliative care research [12]. Given our recruitment strategy for both the pilot survey and case series, screened patient consent was required prior to being contacted by the study coordinator; the reasons for declining consent, and whether or not these patients met the study eligibility criteria, were not consistently documented. In a longitudinal RCT of an educational intervention in 461 palliative care patients, Abernethy et al. (2006) reported that only 31% of the screened population was actually eligible for study inclusion; only 46% of enrolled participants completed follow-up assessments at the end of the 8-week intervention [13]. Clearly further research is warranted in order to determine why patients refuse to be contacted for research and whether they would be eligible as participants within our current local recruitment strategy.

Although the majority of survey participants reported favorably on their perception of ability to participate in a physical activity program, the actual physical ability to participate may decline rapidly in patients with such short life expectancy; over the course of a six-week intervention, symptom burden and physical well-being of end stage cancer patients can fluctuate on a daily basis, such that both adherence and retention to the program can be affected. In a multicenter RCT comparing the effects of cannabinoids on appetite and quality of life in 164 advanced cancer patients, Strasser et al. (2006) reported a 33% dropout rate over the course of their 6-week intervention; the most common reason for dropout was withdrawn consent, which the authors partially attributed to "the clinical reality of interfering symptoms and

complications" in this patient population [14]. Given the challenges of patient attrition within this population, future physical activity intervention trials may benefit from a multicenter approach in order to be adequately powered to determine efficacy for the outcomes of interest.

V-2. FUTURE RESEARCH DIRECTIONS

Given the previously described challenges of study selection inclusion criteria, future research is required into establishing a standardized definition of palliative patients in oncology. Particularly for the systematic review, consensus on the description of palliative research populations is crucial in order to facilitate inter-study comparison and quantitative analysis. In lieu of clinician estimates, use of a validated prognostic tool may aid in defining the patient population more precisely. Broadening the prognostic criteria to include participants with an estimated life expectancy beyond 12 months may enhance accrual, but at the same time may add even further clinical heterogeneity to the study sample.

Other than defining the participant inclusion criteria by life expectancy, it may be worthwhile to categorize participants by palliative performance status level. The palliative performance status (PPS) scale has been widely used and validated in palliative care, and has been shown to be predictive of prognosis in palliative cancer populations [3]; hence targeting cancer patients with a specific PPS level, irrespective of cancer diagnosis or estimated life expectancy, may facilitate recruitment and add a unique dimension to physical activity intervention research in cancer.

Consensus is also required on standardized physical function assessment tools for the palliative cancer population. Although the abbreviated LLFDI is

comprehensive and addresses key physical functioning domains that are endemic in frail populations, it has neither been tested nor validated in palliative cancer patients. Side-by-side comparison of the LLFDI with other physical functioning assessment tools in this population may help define the specific domains which are most significant at the end stages of cancer. Correlation with objective tests of physical functioning would also minimize the potential for error and bias in outcome measurement.

Another potential avenue for investigation would be further pilot testing of the objective measurement of physical activity behavior using the *activ*PAL™ accelerometer. Given our current local recruitment strategy, it would be informative to explicitly characterize the physical activity behavior of patients screened from both the Cross Cancer Institute and the Regional Palliative Home Care program, by correlating self-report with objective accelerometry data. We could therefore examine associations between physical activity behavior, performance status and actual survival in order to further delineate potential subgroups of palliative cancer patients that would best be suited for a physical activity intervention.

For the case series, it is possible that participants declined to be contacted for the study because of the number of exercises and outcome assessments involved. The poor health status of many palliative cancer patients may make them unwilling to participate in lengthy, complicated procedures over extended periods of time [12]; the use of simple, brief and user-friendly assessment tools and interventions may make research studies more appealing to this population. For example, conducting a controlled trial on a single exercise such as sit-to-stand, where the maneuver is simple

to perform and easy to assess as an objective measure of physical functioning, may be more feasible in palliative cancer patients. In addition, limiting the outcome assessments to just key symptoms, such as fatigue using the Brief Fatigue Inventory, instead of assessing all symptoms via the ESAS, may facilitate adherence and retention.

V-3. CONCLUSIONS

The primary objective of the systematic review was to examine the best available evidence on physical activity interventions in this population. There is preliminary evidence to show that at least some palliative cancer patients are willing and able to participate in physical activity interventions, and that physical activity appears to positively impact some supportive care outcomes. The number of studies are few, however, and further pilot studies are required in order to establish feasibility.

The primary objective of the pilot survey was to examine the physical activity preferences, interests and quality of life associations of palliative cancer patients. The majority of respondents reported being willing and feeling able to participate in physical activity, with a strong preference for home-based and solo programs. Moreover, those respondents who reported greater levels of physical activity were associated with higher quality of life scores. Future physical activity intervention trials are warranted to test the hypothesis that physical activity positively affects quality of life in palliative cancer patients, and their unique programming interests and preferences should be incorporated into the development of future physical activity programs in this population.

The primary objective of the case series was to examine the initial development and feasibility testing of a home-based physical activity program in palliative cancer patients. Select palliative cancer patients were able to complete the physical activity intervention safely and with high adherence, and two of the three participants reported improved quality of life scores post-intervention. Eventually a larger intervention trial with bigger sample size and control group is needed to confirm these findings.

This thesis, together with the current evidence base, suggests a promising role for physical activity as a supportive care intervention in palliative cancer patients, but more feasibility research needs to be done. Our studies add to the emerging evidence of feasibility of physical activity in palliative cancer patients. Physical activity interventions in this population are in their infancy and despite positive preliminary evidence, further research is clearly warranted.

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APPENDIX III-1

PILOT SURVEY QUESTIONNAIRE

The following questions relate to your quality of life over the <u>past week</u>. Your answers should indicate the most accurate reply for the <u>majority</u> of days and nights in the <u>past week</u>.

1. Considering ALL parts of my life – physical, emotional, spiritual, and financial – over the past 7 days the quality of my life has been:

_____

0 1 2 3 4 5 6 7 8 9 10
Very Bad *Excellent*

2. Please describe the things which had the greatest effect, positive or negative, on your quality of life in the past 7 days.

_____
_____
_____
_____
_____

3. Over the past 7 days, one troublesome symptom has been: _____

_____

0 1 2 3 4 5 6 7 8 9 10
Very Bad *Excellent*

   a. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____
_____
_____

4. Over the past 7 days, another troublesome symptom has been:

_____

_____

0 1 2 3 4 5 6 7 8 9 10
Very Bad *Excellent*

a. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____
_____
_____

5. Over the past 7 days, a third troublesome symptom has been:

_____

_____

0 1 2 3 4 5 6 7 8 9 10
Very Bad *Excellent*

a. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____
_____
_____

6. Over the past 7 days, I have felt:

_____

0 1 2 3 4 5 6 7 8 9 10
Physically Terrible *Physically Well*

7. Over the past 7 days, how much of the time did you feel sad?

0	1	2	3	4	5	6	7	8	9	10
Never										*Always*

8. Over the past 7 days, when I thought of the future, I was:

0	1	2	3	4	5	6	7	8	9	10
Not Afraid										*Terrified*

9. Over the past 7 days, my life has been:

0	1	2	3	4	5	6	7	8	9	10
Utterly Meaningless And Without Purpose										*Very Purposeful And Meaningful*

10. Over the past 7 days, when I thought about my whole life, I felt that in achieving life goals I have:

0	1	2	3	4	5	6	7	8	9	10
Made No Progress Whatsoever										*Progressed To Complete Fulfillment*

11. Over the past 7 days, when I thought about my life, I felt that my life to this point has been:

0	1	2	3	4	5	6	7	8	9	10
Completely Worthless										*Very Worthwhile*

12. Over the past 7 days, I have felt that I have:

0	1	2	3	4	5	6	7	8	9	10
No Control Over My Life										*Complete Control Over My Life*

13. Over the past 2 days, I felt good about myself as a person:

0	1	2	3	4	5	6	7	8	9	10
Completely Disagree										*Completely Agree*

14. To me, the past 7 days were:

0	1	2	3	4	5	6	7	8	9	10
A Burden										*A Gift*

15. Over the past 7 days, the world has been:

0	1	2	3	4	5	6	7	8	9	10
An Impersonal Unfeeling Place								*Caring and Responsive To My Needs*		

16. Over the past 7 days, I have felt supported:

0	1	2	3	4	5	6	7	8	9	10
Not At All										*Completely*

Below is a list of common symptoms that other people with advanced cancer have identified as important to their quality of life. Please indicate the extent to which you have experienced each of the symptoms during the past week by circling the appropriate number on the following scale.

PLEASE NOTE: The scales below are REVERSED compared to items above.

17. For the following symptoms that have NOT been discussed previously in this questionnaire:

    a. Please rate the number that best describes:

0	1	2	3	4	5	6	7	8	9	10
No Pain										*Worst Possible Pain*

    i. Has the above symptom affected your day-to-day function and activities? If so, how?

    _____
    _____
    _____
    _____
    _____

    b. Please rate the number that best describes:

0	1	2	3	4	5	6	7	8	9	10
Not Tired										*Worst Possible Tiredness*

    i. Has the above symptom affected your day-to-day function and activities? If so, how?

    _____
    _____
    _____
    _____
    _____

c. Please rate the number that best describes:

0	1	2	3	4	5	6	7	8	9	10
Not Nauseated										*Worst Possible Nausea*

i. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____
_____
_____

d. Please rate the number that best describes:

0	1	2	3	4	5	6	7	8	9	10
Not Depressed										*Worst Possible Depression*

i. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____
_____
_____

e. Please rate the number that best describes:

0	1	2	3	4	5	6	7	8	9	10
Not Anxious										*Worst Possible Anxiety*

i. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____

f. Please rate the number that best describes:

0 1 2 3 4 5 6 7 8 9 10
Not Drowsy *Worst Possible Drowsiness*

i. Has the above symptom affected your day-to-day function and activities? If so, how?

g. Please rate the number that best describes:

0 1 2 3 4 5 6 7 8 9 10
Best Appetite *Worst Possible Appetite*

i. Has the above symptom affected your day-to-day function and activities? If so, how?

h. Please rate the number that best describes:

0	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*
Best Feeling Of Wellbeing										*Worst Possible Feeling of Wellbeing*

i. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____
_____
_____

i. Please rate the number that best describes:

0	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*
No Shortness Of Breath										*Worst Possible Shortness of Breath*

i. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____
_____
_____

This next part of the questionnaire is needed to help understand your level of physical activity.

18. Over the past month, I would generally rate my activity as:
    a. Normal with no limitations
    b. Not my normal self, but able to be up and about with fairly normal activities
    c. Not feeling up to most things, but in bed or chair less than half the day
    d. Able to do little activity and spend most of the day in bed or chair
    e. Pretty much bedridden, rarely out of bed

19. Over the past 7 days, my most common physical activity was _____.

    a. On average per week, how often would you perform this activity?
    _____
    b. On average, for how long did you perform this activity each time?
    _____
    c. How strenuous is it for you to perform this activity? (light / moderate / heavy) Why?
    _____
    d. What do you enjoy most about doing this activity?
    _____

20. Over the past 7 days, my 2nd most common physical activity was _____.

    a. On average per week, how often would you perform this activity?
    _____
    b. On average, for how long did you perform this activity each time?
    _____
    c. How strenuous is it for you to perform this activity? (light / moderate / heavy) Why?
    _____
    d. What do you enjoy most about performing this activity?
    _____

21. Over the past 7 days, my 3rd most common physical activity was _____.

    a. On average per week, how often would you perform this activity?
    _____
    b. On average, for how long did you perform this activity each time?
    _____
    c. How strenuous is it for you to perform this activity? (light / moderate / heavy) Why?
    _____
    d. What do you enjoy most about performing this activity?
    _____

This next part of the questionnaire is needed to help understand your level of Physical function. Please rate the difficulty you have with doing the following activities at the present time:

22. How much difficulty do you have:

a. Unscrewing the lid off a previously unopened jar without using any assistive devices?

0	1	2	3	4	5
None					*Cannot Do*

b. Running ½ mile or more?

0	1	2	3	4	5
None					*Cannot Do*

c. Using common utensils for preparing meals (eg. Can opener, potato peeler, or sharp knife)?

0	1	2	3	4	5
None					*Cannot Do*

d. Holding a full glass of water in one hand?

0	1	2	3	4	5
None					*Cannot Do*

e. Walking a mile, taking rests as necessary?

0	1	2	3	4	5
None					*Cannot Do*

f. Going up and down a flight of stairs outside, without using a handrail?

0	1	2	3	4	5
None					*Cannot Do*

g. Ripping open a package of snack food (eg. cellophane wrapping on crackers) using only your hands?

0	1	2	3	4	5
None					*Cannot Do*

h. Pouring from a large pitcher?

0	1	2	3	4	5
None					*Cannot Do*

i. Getting into and out of a car/taxi?

0	1	2	3	4	5
None					*Cannot Do*

j. Going up and down 3 flights of stairs inside, using a handrail?

0	1	2	3	4	5
None					*Cannot Do*

k. Picking up a kitchen chair and moving it, in order to clean?

0	1	2	3	4	5
None					*Cannot Do*

l. Using a step stool to reach into a high cabinet?

0	1	2	3	4	5
None					*Cannot Do*

m. Carrying something in both arms while climbing a flight of stairs (eg. Laundry basket)?

0	1	2	3	4	5
None					*Cannot Do*

n. Bending over from a standing position to pick up a piece of clothing from the floor?

0	1	2	3	4	5
None					*Cannot Do*

o. Walking around one floor of your home, taking into consideration doors, furniture, and a variety of floor coverings?

0	1	2	3	4	5
None					*Cannot Do*

The following questions ask you to rate how you feel about performing a regular physical activity over the next month. Please pay careful attention to the words at each end of the scale and circle the number that best represents how you feel. Please answer all items from (a) to (f).

23. I think that for me to perform regular physical activity over the next month would be:

a.

1	2	3	4	5	6	7
extremely useless	quite useless	slightly useless		slightly useful	quite useful	extremely useful

b.

1	2	3	4	5	6	7
extremely unenjoyable	quite unenjoyable	slightly unenjoyable		slightly enjoyable	quite enjoyable	extremely enjoyable

c.

1	2	3	4	5	6	7
extremely harmful	quite harmful	slightly harmful		slightly beneficial	quite beneficial	extremely beneficial

d.

1	2	3	4	5	6	7
extremely painful	quite painful	slightly painful		slightly pleasurable	quite pleasurable	extremely pleasurable

e.

1	2	3	4	5	6	7
extremely unimportant	quite unimportant	slightly unimportant		slightly important	quite important	extremely important

f.

1	2	3	4	5	6	7
extremely boring	quite boring	slightly boring		slightly fun	quite fun	extremely fun

This next set of questions ask you to rate how other people in your life may feel about you performing regular physical activity over the next month. Please pay careful attention to the words at the end of each scale and circle the number that best represents how they might feel. Please answer all items from (a) to (c).

24. I think that if I engaged in regular physical activity over the next month, most people who are important to me would be:

a.

1	2	3	4	5	6	7
extremely disapproving	quite disapproving	slightly disapproving		slightly approving	quite approving	extremely approving

b.

1	2	3	4	5	6	7
extremely discouraging	quite discouraging	slightly discouraging	encouraging	slightly encouraging	quite encouraging	extremely encouraging

c.

1	2	3	4	5	6	7
extremely unsupportive	quite unsupportive	slightly unsupportive		slightly supportive	quite supportive	extremely supportive

This next question asks you to rate how physically active you think other people in your life are likely to be over the next month.

25. I think that over the next month, most people who are important to me will themselves be:

a.

1	2	3	4	5	6	7
extremely inactive	quite inactive	slightly inactive		slightly active	quite active	extremely active

26. I think that over the next month, most people who are important to me will themselves be physically active regularly.

	1	2	3	4	5	6	7
a.	strongly disagree	moderately disagree	slightly disagree		slightly agree	moderately agree	strongly agree

These next questions ask you to rate how likely you feel it is that you will be able to do regular physical activity over the next month if you were really motivated. Pay careful attention to the words at the end of each scale and circle the number that best represents how you feel.

If you were really motivated....

27. How controllable would it be for you to do regular physical activity over the next month?

	1	2	3	4	5	6	7
a.	extremely uncontrollable	quite uncontrollable	slightly uncontrollable		slightly controllable	quite controllable	extremely controllable

28. How confident would you be that you could do regular physical activity over the next month?

	1	2	3	4	5	6	7
a.	extremely unconfident	quite unconfident	slightly unconfident		slightly confident	quite confident	extremely confident

These next set of questions ask you about your motivation and plans to exercise regularly over the next month. Pay careful attention to the words at the end of each scale.

29. How motivated are you to perform regular physical activity over the next month?

	1	2	3	4	5	6	7
a.	extremely unmotivated	quite unmotivated	slightly unmotivated		slightly motivated	quite motivated	extremely motivated

30. How committed are you to doing regular physical activity over the next month?

a.	1	2	3	4	5	6	7
	extremely uncommitted	quite uncommitted	slightly uncommitted		slightly committed	quite committed	extremely committed

31. I intend to do regular physical activity over the next month:

a.	1	2	3	4	5	6	7
	strongly disagree	moderately disagree	slightly disagree		slightly agree	moderately agree	strongly agree

32. How much regular physical activity do you intend to do over the next month?

_____

This next set of questions asks you about your physical activity preferences.

33. What does being physically active mean to you?

_____
_____
_____
_____
_____

34. Is being physically active important to you **now**? If so, why or why not?

_____
_____
_____
_____
_____

35. Are you interested in a physical activity program **now**?

_____ *Yes* _____ *No* _____ *Maybe/Unsure*

a. If so, why or why not?

_____
_____
_____
_____

36. Do you think you would be able to participate in a physical activity program **now**?

_____ *Yes* _____ *No* _____ *Maybe/Unsure*

a. If so, why or why not?

_____
_____
_____
_____

37. If you were to begin a physical activity program, who would you like to participate with?

_____ *Alone* _____ *Caregiver/Spouse*
_____ *Family/Friends*

_____ *Other Cancer Patients* _____ *No Preference*

38. If I were to begin a physical activity program, where would you like to participate:

_____ *At Home* _____ *At a Hospital-Based Center*

_____ *At a Cancer Center* _____ *At a Local Fitness Center*

_____ *No Preference*

39. If you were to begin a physical activity program, would you prefer to participate in the:

_____ *Morning* _____ *Afternoon* _____ *Evening*

_____ *No Preference*

40. If you were to begin a physical activity program, how long do you think you would be able to participate?

_____ *Less than 10 min* _____ *10-20 min* _____ *20-30 min*

_____ *Over 30 min* _____ *Not at all*

41. If you were to begin a physical activity program, how often would you be interested in participating?

_____

42. My **favorite** physical activity is: _____

43. What type of physical activity would you be most interested in **now**?

_____
_____
_____
_____

PLEASE NOTE: The following questions will be asked if required medical and demographic information CANNOT be determined from the patient's medical record.

The following questions are needed to help understand the medical characteristics of the people participating in the study. For this reason it is very important information. All information is held in strict confidence and its presentation to the public will be group data only. Please answer the questions to the best of your knowledge. Please indicate if you don't know the answer to a specific question.

44. When were you diagnosed with cancer (month/year)? _____

45. What type of cancer do you have?

_____

46. Has the cancer spread anywhere else in your body? If so, where?

_____
_____
_____

47. Did your treatment include surgery? When?

_____
_____
_____

48. Did your treatment include radiation therapy? When? Are you still receiving radiation therapy?

_____
_____
_____

49. Did your treatment include chemotherapy? If yes, how many courses of chemotherapy did you have? Are you still receiving chemotherapy?

_____
_____
_____

50. Have you ever had a recurrence of your cancer? If yes, how many times have you had a recurrence?

_____
_____
_____

51. How long have you been told, by your doctor, that you have left to live? When were you told this?

_____
_____
_____
_____

PLEASE NOTE: The following questions will be asked if required medical and demographic information CANNOT be determined from the patient's medical record.

The next part of the questionnaire is needed to help understand the demographic characteristics of the people participating in the study. For this reason it is very important information. All information is held in strict confidence and its presentation to the public will be group data only. You may refrain from answering the following questions at any time.

52. Age: _____

53. My height is about _____ feet / inches tall (or _____ cm)

54. My current weight is about _____ pounds (or _____ kg)

55. Marital Status

Never Married_____ Married _____ Common Law _____
Separated _____ Widowed _____ Divorced _____

56. Education level _____

57. Annual Family Income

<20,000 _____ 20-39,999 _____ 40-59,999 _____
60-79,999 _____ 80-99,999 _____ >100,000 _____

58. Current Employment Status

Disability _____ Retired _____ Part Time _____
Homemaker _____ Full Time _____
Temporarily Unemployed _____

59. Ethnic origin/ancestry _____

The next set of questions ask you about your current health. This information is to help us understand other important health issues.

60. Current smoking status:

____Never Smoked _____ Ex Smoker _____ Occasional Smoker
_____ Regular smoker (list pk-days)

61. CAGE score: /4

62. Has a doctor or nurse ever told you that you had any of the following conditions?

High blood pressure _____ High cholesterol _____
Heart attack _____ Stroke_____
Emphysema _____ Chronic Bronchitis _____
Diabetes _____ Other Cancer _____
Angina (chest pains) _____ Arthritis _____
Any other long term health conditions _____

APPENDIX III-2

PILOT SURVEY CONSENT FORM

ETH-23009: A PILOT STUDY TO EXPLORE THE ROLE OF PHYSICAL ACTIVITY AS A QUALITY OF LIFE INTERVENTION IN ADVANCED CANCER PATIENTS

A study to explore the role of physical activity in patients with advanced cancer

CONSENT FORM

This form is part of the process of informed consent. It is designed to explain this research study and what will happen to you if you choose to be in this study.

If you would like to know more about something mentioned in this consent form, or have any questions at anytime regarding this research study, please be sure to ask the research nurse or the study coordinator (Sonya Lowe 492-2829). Read this consent form carefully to make sure you understand all the information it provides. You will get a copy of this consent form to keep. You do not have to take part in this study and your care does not depend on whether or not you take part.

Your participation in this study is entirely voluntary. Please take your time to make your decision. It is recommended that you discuss with your friends and/or family about whether to participate in this study.

"WHY IS THIS STUDY BEING DONE?"

You are being asked to take part in this study because you have advanced cancer. Recent research has shown that physical activity may be beneficial for advanced cancer patients. This study is interested in exploring the role of physical activity during your illness and its relationship to quality of life. This is the first study to examine the physical activity preferences, interests and needs of advanced cancer patients.

This study is being done because at present, we do not know if physical activity is beneficial at your stage of cancer. It is important to test this in a study so that doctors and nurses are able to advise

patients about the potential benefits or risks of physical activity at your stage of cancer.

"WHAT DO WE HOPE TO LEARN?"

This study is a pilot study that will lead to a larger study in the future if the results are encouraging. We hope to learn what the specific physical activity needs and interests of patients with advanced cancer are. The objectives of this study are 1) to describe the physical activity preferences of advanced cancer patients 2) to examine the relationship between quality of life and physical activity in advanced cancer patients and 3) to identify which advanced cancer patients would be willing and able to participate in a physical activity intervention.

"WHAT IS INVOLVED IN THIS STUDY?"

If you agree to participate in this research study, you will be asked to sign this consent form, and complete six questionnaires in an interview. The interview will take approximately 45 minutes to complete. If any of the questions ask for information that you are not comfortable in providing, please feel free to skip question(s) and move on to the next question. Your medical record will also be reviewed.

"HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?"

About 30 people will take part in this study at the Cross Cancer Institute and Regional Palliative Home Care Program.

"WHAT WILL MY PARTICIPATION INVOLVE?"

If you take part in this study, a researcher will visit you once and administer six questionnaires by interview. During the interview, you will be asked about your quality of life, your current symptoms, and your level of physical function. The researcher will ask you about your experience with physical activity.

"HOW LONG WILL I BE INVOLVED IN THE STUDY?"

You may be in this study for as long as 45 minutes or until you and the researcher have completed the questionnaires.

"WHAT ARE THE SIDE EFFECTS?"

Some possible risks are involved if you choose to participate in this study. We will be asking you to recall your cancer experience, which for some may be traumatic. If this is problematic for you, you need not participate. If you would like someone to speak to about your cancer experience, you may contact the Department of Psychosocial and

Spiritual Resources at the Cross Cancer Institute at (780) 432-8703/(780) 432-8771 (switchboard).

"WHAT ARE MY ALTERNATIVES?"

You may choose not to participate in this study. This will not impact your cancer treatment or care.

"ARE THERE ANY BENEFITS TO PARTICIPATING IN THIS STUDY?"

Participation in this study may or may not be of personal benefit to you. However, based on the results of this study, it is hoped that, in the long-term, patient care can be improved.

"CAN I WITHDRAW FROM THIS STUDY?"

Taking part in this study is voluntary; you may withdraw from the study at any time if you wish to do so. Should you decide to withdraw from the study at any time, information collected on you up until that point would still be provided to the study co-ordinator.

"ARE THERE COSTS TO ME FOR TAKING PART IN THIS STUDY?"

There are no additional costs to you for taking part in this study.

"WHAT ARE MY RIGHTS AS A PARTICIPANT?"

If you suffer an injury or become ill as a result of participating in this research, you will receive all medical treatments (or services) recommended by your doctors that are not covered by health insurance. No compensation will be provided beyond this point. However, it is important to note that nothing said in this consent form alters your legal rights to recover damages.

"WILL MY PERSONAL INFORMATION BE KEPT CONFIDENTIAL?"

Identifiable health information will be collected during this study. This information may be used by the researchers who are carrying out this study, and may be disclosed to others as described below. Any research proposal to use information that identifies you for a purpose other than this study must be approved in advance by the ACB Research Ethics Board.

Direct access to your identifiable health information collected for this study will be restricted to the researchers who are directly involved in this study except in the following circumstances:

Your identifiable health information may need to be inspected or copied from time to time for quality assurance (to make sure the information being used in the study is accurate) and for data analysis (to do statistical analysis that will not identify you). The following organizations may do this inspection:

- Alberta Cancer Board Research Ethics Board, the institutional review board at this centre
- Health Canada

Any disclosure of your identifiable health information will be in accordance with the Alberta Health Information Act. As well, any person from the organizations looking at your records on-site at the Cross Cancer Institute will follow the relevant Alberta Cancer Board policies and procedures that control these actions. Any disclosure of your identifiable health information to another individual or organization not listed here will need the approval of the Alberta Cancer Board Research Ethics Board.

Your identifiable health information collected as part of this study which includes records of your progress and your responses to the questionnaire will be kept confidential in a secure facility.

The researchers who are directly involved in your study may share information about you with other researchers, but you will not be identified in that shared information except by a number. The key that indicates what number you have been assigned will be kept secure by the researchers directly involved with your study and will not be released.

Although absolute confidentiality can never be guaranteed, the Alberta Cancer Board will make every effort to keep your identifiable health information confidential, and to follow the ethical and legal rules about collecting, using and disclosing this information in accordance with the Alberta Health Information Act and other regulatory requirements.

"WHO DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?"

You may contact the Principal Investigator (Kerry Courneya, 492-1031) or the study coordinator (Sonya Lowe, 492-2829) to answer any questions you have about this study.

If you feel, at any time, that you have not been informed to your satisfaction about the risks, benefits, or alternatives of this study, or that you have been encouraged to continue in this study after you wanted to withdraw, you can call the Patient Representative at (780) 432-8585.

UNDERSTANDING OF PARTICIPANTS

I can refuse to take part or withdraw from this study at any time without jeopardizing my health care. If I continue to take part in the study, I will be kept informed of any

important new developments and information learned after the time I gave my original consent.

I also give consent for the Principal Investigator and the Alberta Cancer Board (the Custodian) to disclose identifiable health information, as per the Alberta Health Information Act, to the organizations mentioned on the previous page.

I have read and understood all of the information in this consent form. I have asked questions, and received answers concerning areas I did not understand. I have had the opportunity to take this consent form home for review and discussion. My consent has not been forced or influenced in any way. I consent to participate in this research study. Upon signing this form I will receive a signed copy of the consent.

(PRINT NAMES CLEARLY)

Name of Patient	Signature of Patient	Date &Time
Name of Witness	Signature of Witness	Date & Time
Name of Person Obtaining Consent	Signature of Person Obtaining Consent	Date & Time
Name of Investigator	Signature of Investigator	Date & Time

APPENDIX III-3

PILOT SURVEY PARTICIPANT INFORMATION LETTER

PHYSICAL ACTIVITY IN ADVANCED CANCER

It is important for us to understand the role of physical activity during your illness. Currently we do not know how physical activity and your quality of life are related in people with advanced cancer. This study will examine whether physical activity programs could be used to improve quality of life during your illness.

WHAT DO WE HOPE TO LEARN?

We hope to learn more about the role that physical activity plays during your illness. The goal of this study is to find out whether physical activity could be used to improve your quality of life. We also want to learn about the types of physical activity programs that might be of interest to you. Even if you are not interested in any physical activity, we would like to learn why and for what reason.

WHAT WILL MY PARTICIPATION INVOLVE?

A researcher will visit you once and administer six questionnaires by interview. During the interview, you will be asked about your quality of life, your current symptoms, and your level of physical function. The researcher will ask you about your experience with physical activity.

You may be in this study for as long as 45 minutes or until you and the researcher have completed the interview. The interview will be arranged at your convenience, at the Cross Cancer Institute, one of the Edmonton-area hospitals/hospices, or in your home.

CONTACT:

Sonya Lowe, Study Coordinator. (T) 492-2829

APPENDIX III-4

PILOT SURVEY ETHICAL APPROVAL

Alberta Cancer Board

Provincial Office
1200, Standard Life Building
10405 Jasper Avenue
Edmonton, Alberta
Canada T5J 3N4
Tel: (780) 412-4000

ACB Provincial Office
Edmonton

Tertiary Cancer Centres
Cross Cancer Institute
Tom Baker Cancer Centre

Associate Cancer Centres
Central Alberta Cancer Centre
(Red Deer)
Grande Prairie Cancer Centre
Lethbridge Cancer Centre
Medicine Hat Cancer Centre

Community Cancer Centres
Banff
Bonnyville
Camrose
Canmore
Drayton Valley
Drumheller
Ft. McMurray
High River
Hinton
Lloydminster
Peace River

Division of Population Health and Information
Calgary

Medical Affairs and Community Oncology
Edmonton

Research
Edmonton

Alberta Cancer Foundation
Accepts donations in support of ACB facilities and programs
Toll-free: 1-866-412-4222

www.cancerboard.ab.ca

ALBERTA CANCER BOARD

10 October 2006

Dr. Kerry Courneya
Faculty of Physical Education
University of Alberta

Dear: Dr. Courneya,

RE: ETH-23002: A Pilot Study to Explore the Role of Physical Activity as a Quality of Life Intervention in Advanced Cancer Patients

The Research Ethics Board (full board) met on 12 September 2006 to discuss the above protocol. Thank you for your response to my correspondence dated 15 September 2006. I am pleased to grant approval to your participation in the above noted study on behalf of the Research Ethics Board (REB). The following documents have been reviewed and approved as of 21 April 2006:

- Protocol including Survey Questionnaire (Version 2.0 dated 2 October 2006)
- Consent Form (received 4 October 2006)

Please note that this approval is based on the following conditions:

- a copy of the informed consent form must be given to each research subject and consent obtained prior to enrollment on the study;
- if there are any other changes to the protocol or consent form during the year, or if any serious adverse events to the treatment are found, a letter describing the changes/reactions must be forwarded to the REB as per the Alberta Cancer Board Policy J3.11b together with an updated consent form;
- an Annual Renewal form must be submitted two months prior to the deadline date of **12 September 2007** (one year from date of the convened REB meeting), containing the information as per our annual renewal form;
- a Final Report must be submitted at the termination of the project.

The deliberations of the REB included all elements described in Section 50 of the Health Information Act, and found the study to be in compliance with all the applicable requirements of the Act. The REB determined that consent will be obtained from study participants for disclosure of the health information to be used in the research.

The Alberta Cancer Board REB, complies with the following guidelines and regulations:

- Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans;

- Health Information Act which has been proclaimed on April 25, 2001 in Alberta;
- Health Canada, as defined in C.05 (Part C Division 5) (1024-Clinical Trials) of the Food And Drug Regulations-Amendment and the Therapeutic Products Directorate Guidelines/ICH Harmonized Tripartite Guidelines-Good Clinical Practice: Consolidate Guidelines;
- National Institutes of Health-Code of Federal Regulations (USA); and
- Our institution has been approved by the Office for Human Research Protections in the United States.

Members of the REB who are named as investigators or co-investigators in research studies do not participate in discussion related to, nor vote on, such studies when they are presented to the REB.

Please accept the Board's best wishes for success in your research.

Sincerely,

Scott North, M.D.
Chair, Research Ethics Board

/jg

PC:
CPA
Brenda Bird-Cantelon
OIPC

Health Research Ethics Board

213 Heritage Medical Research Centre
University of Alberta, Edmonton, Alberta T6G 2S2
p. 780.492.9726 (Biomedical Panel)
p. 780.492.0802 (Health Panel)
p. 780.492.0439
p. 780.492.0839
f. 780.492.2808

December 7, 2006

Dr. Kerry Courneya
Behavioral Medicine Laboratory
Faculty of Physical Education
E-488 Van Vliet Centre

Dear Dr. Courneya:

Re: **A pilot study to explore the role of physical activity as a quality of life intervention in advanced cancer patients**

Thank you for submitting this application for reciprocal approval.

The Alberta Cancer Board (ACB) REB last approved the above named protocol on October 10, 2006. That approval has been accepted by the University of Alberta and by its Health Research Ethics Board, and a signed document is enclosed for your records.

The ACB REB will remain your REB-of-record.

Yours sincerely,

Judith R. Abbott
Senior Coordinator
Health Research Ethics Board (Biomedical Panel)

/ja
enc.

I. University of Alberta Institutional Authorization to Accept Alberta Cancer Board Research Ethics Board (REB)[1] Approval of an Ethics Application

II. University of Alberta Health Research Ethics Board (HREB) Acceptance of the Alberta Cancer Board REB Approval of the application titled "A pilot study to explore the role of physical activity as a quality of life intervention in advanced cancer patients", submitted by Dr. Kerry Courneya

I. Institutional Authorization

The University of Alberta authorizes its HREB to accept the Alberta Cancer Board REB approval of the above named ethics application. This authorization is made pursuant to the *Tri-Council Policy Statement* amendment that permits "[a]n institution...[to]...authorize its REB(s) to accept the review of other REBs constituted under the Tri-Council Policy Statement."[2] Via its deemed amendment clause, the *University of Alberta Standards for the Protection of Human Research Participants* (GFC 66) permits this authorization.[3]

Vice-President (Research), University of Alberta
Dr. G. Kachanoski

Dec. 5, 2006
Date

Acting Chair, University Committee on Human Research Ethics
Dr. W.A. McBlain

Nov 23/06
Date

II. HREB Acceptance

The University of Alberta HREB accepts the Alberta Cancer Board REB approval of the ethics application titled "**A pilot study to explore the role of physical activity as a quality of life intervention in advanced cancer patients**", for Dr. Kerry Courneya

Chair, University of Alberta HREB (Health Panel)
Dr. Glenn G. Griener

27 November 2006
Date

[1] Also referred to as the "Alberta Cancer Board *Research Ethics Committee*."

[2] Revision and amendment to Article 1.2, B1, Section 1, Ethics Review, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, stating that "Each institution is accountable for the research carried out in its own jurisdiction or under its auspices. An institution can authorize its REB(s) to accept the review of other REBs constituted under the Tri-Council Policy Statement if it so wishes."

[3] GFC66.1.1 Definitions, Purview of the *UA Standards for the Protection of Human Research Participants* [excerpted], "From time-to-time as the Ethical Principles and/or requirements of the Articles of the Tri-Council Policy [Statement] are revised or amended any such revision or amendment shall be deemed to be an amendment and revision to corresponding sections of the UA Standards."

Filing: Human Research Protections Office; Vice-President (Research); Chair, HREB (A); Chair, HREB (B); Alberta Cancer Board REB.

APPENDIX IV-1

PILOT INTERVENTION BASELINE QUESTIONNAIRE

This questionnaire asks you for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

The following questions relate to your experience of hope. Describe your experience of hope, according to the nine sets of words below. Each set has seven possible answers, with numbers 1 and 7 being the extreme answers. Circle the number which best describes *what the word, hope, means to you.* Please give only one answer for each set. There is no right or wrong answer.

I would like you to think about the word, Hope.
What does the word, hope, mean to you?

	Extremely	Quite	Slightly	Both/Neither	Slightly	Quite	Extremely	
	1	2	3	4	5	6	7	
Tender								*Tough*
Valuable	1	2	3	4	5	6	7	*Worthless*
Disabling	1	2	3	4	5	6	7	*Empowering*
Certain	1	2	3	4	5	6	7	*Uncertain*
Mistrusting	1	2	3	4	5	6	7	*Trusting*
Slow	1	2	3	4	5	6	7	*Fast*
Meaningful	1	2	3	4	5	6	7	*Meaningless*
Expected	1	2	3	4	5	6	7	*Unexpected*
Dishonest	1	2	3	4	5	6	7	*Honest*

The following questions relate to your quality of life over the <u>past week</u>. Your answers should indicate the most accurate reply for the <u>majority</u> of days and nights in the <u>past week</u>.

1. Considering ALL parts of my life – physical, emotional, spiritual, and financial – over the past 7 days the quality of my life has been:

_____

0 1 2 3 4 5 6 7 8 9 10
Very Bad *Excellent*

2. Please describe the things which had the greatest effect, positive or negative, on your quality of life in the past 7 days.

_____
_____
_____
_____
_____

3. Over the past 7 days, one troublesome symptom has been: _____

_____

0 1 2 3 4 5 6 7 8 9 10
Very Bad *Excellent*

   a. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____
_____
_____

4. Over the past 7 days, another troublesome symptom has been:

_____

0	1	2	3	4	5	6	7	8	9	10
Very Bad										*Excellent*

a. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____
_____

5. Over the past 7 days, a third troublesome symptom has been:

_____

0	1	2	3	4	5	6	7	8	9	10
Very Bad										*Excellent*

a. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____
_____
_____

6. Over the past 7 days, I have felt:

0	1	2	3	4	5	6	7	8	9	10
Physically Terrible										*Physically Well*

7. Over the past 7 days, how much of the time did you feel sad?

0	1	2	3	4	5	6	7	8	9	10
Never										*Always*

8. Over the past 7 days, when I thought of the future, I was:

0	1	2	3	4	5	6	7	8	9	10
Not Afraid										*Terrified*

9. Over the past 7 days, my life has been:

0	1	2	3	4	5	6	7	8	9	10
Utterly Meaningless And Without Purpose								*Very Purposeful And Meaningful*		

10. Over the past 7 days, when I thought about my whole life, I felt that in achieving life goals I have:

0	1	2	3	4	5	6	7	8	9	10
Made No Progress Whatsoever										*Progressed To Complete Fulfillment*

11. Over the past 7 days, when I thought about my life, I felt that my life to this point has been:

0	1	2	3	4	5	6	7	8	9	10
Completely Worthless										*Very Worthwhile*

12. Over the past 7 days, I have felt that I have:

0	1	2	3	4	5	6	7	8	9	10
No Control Over My Life										*Complete Control Over My Life*

13. Over the past 2 days, I felt good about myself as a person:

0	1	2	3	4	5	6	7	8	9	10
Completely Disagree										*Completely Agree*

14. To me, the past 7 days were:

0	1	2	3	4	5	6	7	8	9	10
A Burden										*A Gift*

15. Over the past 7 days, the world has been:

0	1	2	3	4	5	6	7	8	9	10
An Impersonal Unfeeling Place								*Caring and Responsive To My Needs*		

16. Over the past 7 days, I have felt supported:

0	1	2	3	4	5	6	7	8	9	10
Not At All										*Completely*

Below is a list of common symptoms that other people with advanced cancer have identified as important to their quality of life. Please indicate the extent to which you have experienced each of the symptoms <u>during the past week</u> by circling the appropriate number on the following scale.

PLEASE NOTE: The scales below are REVERSED compared to items above.

17. For the following symptoms that have NOT been discussed previously in this questionnaire:

a. Please rate the number that best describes:

0 1 2 3 4 5 6 7 8 9 10
No Pain *Worst Possible Pain*

i. Has the above symptom affected your day-to-day function and activities? If so, how?

b. Please rate the number that best describes:

0 1 2 3 4 5 6 7 8 9 10
Not Tired *Worst Possible Tiredness*

i. Has the above symptom affected your day-to-day function and activities? If so, how?

c. Please rate the number that best describes:

0 1 2 3 4 5 6 7 8 9 10
Not Nauseated *Worst Possible Nausea*

i. Has the above symptom affected your day-to-day function and activities? If so, how?

d. Please rate the number that best describes:

0 1 2 3 4 5 6 7 8 9 10

Not Depressed *Worst Possible Depression*

i. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____
_____
_____

e. Please rate the number that best describes:

0 1 2 3 4 5 6 7 8 9 10

Not Anxious *Worst Possible Anxiety*

i. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____
_____
_____

f. Please rate the number that best describes:

0 1 2 3 4 5 6 7 8 9 10

Not Drowsy *Worst Possible Drowsiness*

i. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____
_____
_____

g. Please rate the number that best describes:

0	1	2	3	4	5	6	7	8	9	10
Best Appetite										*Worst Possible Appetite*

i. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____
_____
_____

h. Please rate the number that best describes:

0	1	2	3	4	5	6	7	8	9	10
Best Feeling Of Wellbeing										*Worst Possible Feeling of Wellbeing*

i. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____
_____
_____

i. Please rate the number that best describes:

0	1	2	3	4	5	6	7	8	9	10
No Shortness Of Breath										*Worst Possible Shortness of Breath*

i. Has the above symptom affected your day-to-day function and activities? If so, how?

_____
_____
_____
_____
_____

This next part of the questionnaire is needed to help understand your level of physical activity.

18. Over the past month, I would generally rate my activity as:
    a. Normal with no limitations
    b. Not my normal self, but able to be up and about with fairly normal activities
    c. Not feeling up to most things, but in bed or chair less than half the day
    d. Able to do little activity and spend most of the day in bed or chair
    e. Pretty much bedridden, rarely out of bed

19. Over the past 7 days, my most common physical activity was _____.

    a. On average per week, how often would you perform this activity?
    _____
    b. On average, for how long did you perform this activity each time?
    _____
    c. How strenuous is it for you to perform this activity? (light / moderate / heavy) Why?
    _____
    d. What do you enjoy most about doing this activity?
    _____

20. Over the past 7 days, my 2nd most common physical activity was _____.

    a. On average per week, how often would you perform this activity?
    _____
    b. On average, for how long did you perform this activity each time?
    _____
    c. How strenuous is it for you to perform this activity? (light / moderate / heavy) Why?
    _____
    d. What do you enjoy most about performing this activity?
    _____

21. Over the past 7 days, my 3rd most common physical activity was _____.

    a. On average per week, how often would you perform this activity?
    _____
    b. On average, for how long did you perform this activity each time?
    _____
    c. How strenuous is it for you to perform this activity? (light / moderate / heavy) Why?
    _____
    d. What do you enjoy most about performing this activity?
    _____

This next part of the questionnaire is needed to help understand your level of Physical function. Please rate the difficulty you have with doing the following activities at the present time:

22. How much difficulty do you have:

a. Unscrewing the lid off a previously unopened jar without using any assistive devices?

0	1	2	3	4	5
None					*Cannot Do*

b. Running ½ mile or more?

0	1	2	3	4	5
None					*Cannot Do*

c. Using common utensils for preparing meals (eg. Can opener, potato peeler, or sharp knife)?

0	1	2	3	4	5
None					*Cannot Do*

d. Holding a full glass of water in one hand?

0	1	2	3	4	5
None					*Cannot Do*

e. Walking a mile, taking rests as necessary?

0	1	2	3	4	5
None					*Cannot Do*

f. Going up and down a flight of stairs outside, without using a handrail?

0	1	2	3	4	5
None					*Cannot Do*

g. Ripping open a package of snack food (eg. cellophane wrapping on crackers) using only your hands?

0	1	2	3	4	5
None					*Cannot Do*

h. Pouring from a large pitcher?

0	1	2	3	4	5
None					*Cannot Do*

i. Getting into and out of a car/taxi?

0	1	2	3	4	5
None					*Cannot Do*

j. Going up and down 3 flights of stairs inside, using a handrail?

0	1	2	3	4	5
None					*Cannot Do*

k. Picking up a kitchen chair and moving it, in order to clean?

0	1	2	3	4	5
None					*Cannot Do*

l. Using a step stool to reach into a high cabinet?

0	1	2	3	4	5
None					*Cannot Do*

m. Carrying something in both arms while climbing a flight of stairs (eg. Laundry basket)?

_____

0 1 2 3 4 5

n. Bending over from a standing position to pick up a piece of clothing from the floor?

_____

0 1 2 3 4 5
None *Cannot Do*

o. Walking around one floor of your home, taking into consideration doors, furniture, and a variety of floor coverings?

_____

0 1 2 3 4 5
None *Cannot Do*

This next part of the questionnaire is needed to help understand your level of fatigue.

Throughout our lives, most of us have times when we feel very tired or fatigued. Have you felt unusually tired or fatigued in the last week? _____ Yes _____ No

1. Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your fatigue RIGHT NOW.

0	1	2	3	4	5	6	7	8	9	10
No fatigue										As bad as you can imagine

2. Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your USUAL level of fatigue during past 24 hours.

0	1	2	3	4	5	6	7	8	9	10
No fatigue										As bad as you can imagine

3. Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your WORST level of fatigue during the past 24 hours.

0	1	2	3	4	5	6	7	8	9	10
No fatigue										As bad as you can imagine

4. Circle the one number that describes how, during the past 24 hours, fatigue has interfered with your:

A. General activity

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

B. Mood

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

C. Walking ability

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

D. Normal work (includes both work outside the home and daily chores)

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

E. Relations with other people

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

F. Enjoyment of life

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

The following questions ask you to rate how you feel about performing a regular physical activity over the next month. Please pay careful attention to the words at each end of the scale and circle the number that best represents how you feel. Please answer all items from (a) to (f).

23. I think that for me to perform regular physical activity over the next month would be:

a.

1	2	3	4	5	6	7
extremely useless	quite useless	slightly useless		slightly useful	quite useful	extremely useful

b.

1	2	3	4	5	6	7
extremely unenjoyable	quite unenjoyable	slightly unenjoyable		slightly enjoyable	quite enjoyable	extremely enjoyable

c.

1	2	3	4	5	6	7
extremely harmful	quite harmful	slightly harmful		slightly beneficial	quite beneficial	extremely beneficial

d.

1	2	3	4	5	6	7
extremely painful	quite painful	slightly painful		slightly pleasurable	quite pleasurable	extremely pleasurable

	1	2	3	4	5	6	7
e.	extremely unimportant	quite unimportant	slightly unimportant		slightly important	quite important	extremely important
f.	extremely boring	quite boring	slightly boring		slightly fun	quite fun	extremely fun

This next set of questions ask you to rate how other people in your life may Feel about you performing regular physical activity over the next month. Please pay careful attention to the words at the end of each scale and circle the number that best represents how they might feel. Please answer all items from (a) to (c).

24. I think that if I engaged in regular physical activity over the next month, most people who are important to me would be:

	1	2	3	4	5	6	7
a.	extremely disapproving	quite disapproving	slightly disapproving		slightly approving	quite approving	extremely approving
b.	extremely discouraging	quite discouraging	slightly discouraging		slightly encouraging	quite encouraging	extremely encouraging
c.	extremely unsupportive	quite unsupportive	slightly unsupportive		slightly supportive	quite supportive	extremely supportive

This next question asks you to rate how physically active you think other people in your life are likely to be over the next month.

25. I think that over the next month, most people who are important to me will themselves be:

	1	2	3	4	5	6	7
a.	extremely inactive	quite inactive	slightly inactive		slightly active	quite active	extremely active

26. I think that over the next month, most people who are important to me will themselves be physically active regularly.

	1	2	3	4	5	6	7
a.	strongly disagree	moderately disagree	slightly disagree		slightly agree	moderately agree	strongly agree

These next questions ask you to rate how likely you feel it is that you will be able to do regular physical activity over the next month if you were really motivated. Pay careful attention to the words at the end of each scale and circle the number that best represents how you feel.

If you were really motivated….

27. How controllable would it be for you to do regular physical activity over the next month?

	1	2	3	4	5	6	7
a.	extremely uncontrollable	quite uncontrollable	slightly uncontrollable		slightly controllable	quite controllable	extremely controllable

28. How confident would you be that you could do regular physical activity over the next month?

	1	2	3	4	5	6	7
a.	extremely unconfident	quite unconfident	slightly unconfident		slightly confident	quite confident	extremely confident

These next set of questions ask you about your motivation and plans to exercise regularly over the next month. Pay careful attention to the words at the end of each scale.

29. How motivated are you to exercise regularly over the next month?

	1	2	3	4	5	6	7
a.	extremely unmotivated	quite unmotivated	slightly unmotivated		slightly motivated	quite motivated	extremely motivated

30. How committed are you to doing regular physical activity over the next month?

	1	2	3	4	5	6	7
a.	extremely uncommitted	quite uncommitted	slightly uncommitted		slightly committed	quite committed	extremely committed

31. I intend to do regular physical activity over the next month:

	1	2	3	4	5	6	7
a.	strongly disagree	moderately disagree	slightly disagree		slightly agree	moderately agree	strongly agree

32. How much regular physical activity do you intend to do over the next month?

_____

This next set of questions asks you about your physical activity preferences.

33. What does being physically active mean to you?

_____
_____
_____
_____
_____

34. Is being physically active important to you **now**? If so, why or why not?

_____
_____
_____
_____
_____

PLEASE NOTE: The following questions will be asked if required medical and demographic information CANNOT be determined from the patient's medical record.

The following questions are needed to help understand the medical characteristics of the people participating in the study. For this reason it is very important information. All information is held in strict confidence and its presentation to the public will be group data only. Please answer the questions to the best of your knowledge. Please indicate if you don't know the answer to a specific question.

35. When were you diagnosed with cancer (month/year)? _____

36. What type of cancer do you have?

_____

37. Has the cancer spread anywhere else in your body? If so, where?

_____

_____

_____

38. Did your treatment include surgery? When?

_____

_____

_____

39. Did your treatment include radiation therapy? When? Are you still receiving radiation therapy?

_____

_____

_____

40. Did your treatment include chemotherapy? If yes, how many courses of chemotherapy did you have? Are you still receiving chemotherapy?

_____

_____

_____

41. Have you ever had a recurrence of your cancer? If yes, how many times have you had a recurrence?

_____

_____

_____

42. How long have you been told, by your doctor, that you have left to live? When were you told this?

_____

_____

_____

_____

The next set of questions ask you about your current health. This information is to help us understand other important health issues.

43. Current smoking status:
____Never Smoked _____ Ex Smoker _____ Occasional Smoker
_____ Regular smoker (list pk-days)

44. CAGE score: /4

45. Has a doctor or nurse ever told you that you had any of the following conditions?

High blood pressure _____ High cholesterol _____
Heart attack _____ Stroke_____
Emphysema _____ Chronic Bronchitis _____
Diabetes _____ Other Cancer _____
Angina (chest pains) _____ Arthritis _____
Any other long term health conditions _____

PLEASE NOTE: The following questions will be asked if required medical and demographic information CANNOT be determined from the patient's medical record.

The next part of the questionnaire is needed to help understand the demographic characteristics of the people participating in the study. For this reason it is very important information. All information is held in strict confidence and its presentation to the public will be group data only.

46. Age: _____

47. My height is about _____ feet / inches tall (or _____ cm)

48. My current weight is about _____ pounds (or _____ kg)

49. Marital Status
Never Married_____ Married _____ Common Law _____
Separated _____ Widowed _____ Divorced _____

50. Education level _____

51. Annual Family Income
<20,000 _____ 20-39,999 _____ 40-59,999 _____
60-79,999 _____ 80-99,999 _____ >100,000 _____

52. Current Employment Status
    Disability _____ Retired _____ Part Time _____
    Homemaker _____ Full Time _____
    Temporarily Unemployed _____

53. Ethnic origin/ancestry _____
54. Palliative Performance Scale level: _____
55. Current medication list:

APPENDIX IV-2

PILOT INTERVENTION POST QUESTIONNAIRE

The post-intervention questionnaire will be identical to the baseline questionnaire except for the following changes: 1) demographic variables will be omitted in post-intervention questionnaire 2) medical variables will be omitted in post-intervention questionnaire 3) physical activity history will be omitted in post-intervention questionnaire

For the post-intervention questionnaire, the following self-report items will be in addition to the included baseline self-report items.

The questions in this section ask how you felt about the physical activity program.
Please choose the best answer on the scale below:

1. I think that participating in the physical activity program was…

a.

Extremely useless	Quite useless	Slightly useless	Neutral	Slightly useful	Quite useful	Extremely useful

b.

Extremely unenjoyable	Quite unenjoyable	Slightly unenjoyable	Neutral	Slightly enjoyable	Quite enjoyable	Extremely enjoyable

c.

Extremely boring	Quite boring	Slightly boring	Neutral	Slightly interesting	Quite interesting	Extremely interesting

2. My completing the physical activity program was…

Extremely easy	Quite easy	Slightly easy	Neutral	Slightly difficult	Quite difficult	Extremely difficult

3. How much control do you feel that you had over completing the physical activity program?

Very little Control			Moderate control			Complete control

4. On average, how motivated were you to attend all the physical activity sessions throughout the program?

Slightly Motivated			Moderately motivated			Extremely motivated

5. Having completed the physical activity program, I…

a. relieved my stress

Not at all		somewhat		a fair bit		very much

b. improved my energy level

Not at all		somewhat		a fair bit		very much

c. increased my physical strength

Not at all		somewhat		a fair bit		very much

d. improved my well-being

Not at all		somewhat		a fair bit		very much

e. improved my self-image

Not at all		somewhat		a fair bit		very much

e. lost weight

Not at all		somewhat		a fair bit		very much

f. gained weight

Not at all somewhat a fair bit very much

g. slept more soundly

Not at all somewhat a fair bit very much

h. other (describe): _____

Not at all somewhat a fair bit very much

6. Participating in the physical activity program…

a. took away time that I could have spent on other important things

Not at all somewhat a fair bit very much

b. made me tired and fatigued

Not at all somewhat a fair bit very much

c. made me sore

Not at all somewhat a fair bit very much

d. led to injury

Not at all somewhat a fair bit very much

e. made me eat more

Not at all somewhat a fair bit very much

f. other (describe): _____

Not at all somewhat a fair bit very much

7. Barriers to my participation in the physical activity program were…

a. getting to the fitness centre

Not at all somewhat a fair bit very much

b. weather

Not at all somewhat a fair bit very much

c. lack of motivation

Not at all somewhat a fair bit very much

d. too busy or too little time

Not at all somewhat a fair bit very much

e. feeling tired or fatigued

Not at all somewhat a fair bit very much

f. pain or soreness

Not at all somewhat a fair bit very much

g. medical or health problems (describe): _____

Not at all somewhat a fair bit very much

h. other (describe): _____

Not at all somewhat a fair bit very much

8. How supportive were the following people for your participation in the physical activity program?

a. spouse/partner (if applicable)

Not at all somewhat a fair bit very much

b. caregiver (if different from other individuals listed)

Not at all somewhat a fair bit very much

c. other family members

Not at all somewhat a fair bit very much

d. other patients in the study

Not at all somewhat a fair bit very much

e. trainers at the fitness centre

Not at all somewhat a fair bit very much

f. other study staff (ie. Study coordinator)

Not at all somewhat a fair bit very much

f. other (describe): _____

Not at all somewhat a fair bit very much

9. My participation in the physical activity program was helped by…

a. having access to a fitness centre

Not at all somewhat a fair bit very much

b. having a trainer to tell me what activities to do

Not at all somewhat a fair bit very much

c. knowing that a trainer was expecting me and checking my progress

Not at all somewhat a fair bit very much

d. seeing other participants complete the exercise

Not at all somewhat a fair bit very much

e. wanting to see an improvement in the measures of health and fitness being taken for the study

Not at all somewhat a fair bit very much

f. knowing that I was part of a research study

Not at all somewhat a fair bit very much

g. other (describe): _____

Not at all somewhat a fair bit very much

10. The physical activity program has taught me:

a. at what level I should perform physical activity

Not at all somewhat a fair bit very much

b. how to use exercise equipment

Not at all		somewhat		a fair bit		very much

c. that I have the ability to perform physical activity

Not at all		somewhat		a fair bit		very much

d. to find some form(s) of physical activity that I liked

Not at all		somewhat		a fair bit		very much

e. how to make physical activity a part of my regular routine

Not at all		somewhat		a fair bit		very much

f. how to cope with temporary barriers to performing physical activity

Not at all		somewhat		a fair bit		very much

g. other (describe): _____

Not at all		somewhat		a fair bit		very much

11. I would rate my level of success in the physical activity training program as:

Extremely Unsuccessful	quite unsuccessful	slightly unsuccessful	Neutral	slightly successful	quite successful	extremely successful

12. Now that the physical activity program is over, I think that continuing to exercise would be:

a.

Extremely useless	Quite useless	Slightly useless	Neutral	Slightly useful	Quite useful	Extremely useful

b.

Extremely unenjoyable	Quite unenjoyable	Slightly unenjoyable	Neutral	Slightly enjoyable	Quite enjoyable	Extremely enjoyable

c.

Extremely boring	Quite boring	Slightly boring	Neutral	Slightly interesting	Quite interesting	Extremely interesting

d.

Extremely unimportant	Quite unimportant	Slightly unimportant	Neutral	Slightly important	Quite important	Extremely important

13. For me to continue to perform physical activity would be…

Extremely easy	Quite easy	Slightly easy	Neutral	Slightly difficult	Quite difficult	Extremely difficult

14. How much control do you feel you would have over continuing to perform physical activity?

Very little Control			Moderate control			Completely control

15. How motivated are you to continue performing physical activity?

Extremely Unmotivated	Quite unmotivated	Slightly unmotivated	Neutral	Slightly motivated	Quite motivated	Extremely motivated

16. Most people who are important to me think I should continue to perform physical activity…

Strongly Disagree	Moderately disagree	Slightly disagree	Neutral	Slightly agree	Moderately agree	Strongly agree

17. Most people who are important to me approve of me continuing to exercise…

Strongly Disagree	Moderately disagree	Slightly disagree	Neutral	Slightly agree	Moderately agree	Strongly agree

18. Barriers to my continuing to perform physical activity would be…

a. cost

Not at all somewhat a fair bit very much

b. getting access to a place to perform physical activity

Not at all somewhat a fair bit very much

c. not having a trainer anymore

Not at all somewhat a fair bit very much

d. weather

Not at all somewhat a fair bit very much

e. lack of motivation

Not at all somewhat a fair bit very much

f. too busy or too little time

Not at all somewhat a fair bit very much

g. feeling tired or fatigued

Not at all		somewhat		a fair bit		very much

h. pain or soreness

Not at all		somewhat		a fair bit		very much

i. medical or health problems (describe): _____

Not at all		somewhat		a fair bit		very much

j. other (describe): _____

Not at all		somewhat		a fair bit		very much

19. Now that the physical activity program is over, I plan to perform physical activity, on average…

_____ times per week _____ minutes each time

_____low intensity _____moderate intensity _____high intensity

20. How confident are you that you will exercise at this level over the next few weeks?

Extremely Unconfident	Moderately unconfident	Slightly unconfident	Neutral	Slightly confiden	Moderately confident	Extremely confident

21. I plan to…

a. walk

Yes	No	I don't know

b. do weights

_____	_____	_____
Yes	No	I don't know

c. other (describe): _____

22. I plan to perform physical activity…

a. at home

_____	_____	_____
Yes	No	I don't know

b. at a fitness centre

_____	_____	_____
Yes	No	I don't know

c. outside

_____	_____	_____
Yes	No	I don't know

d. other (describe): _____

APPENDIX IV-3

PILOT INTERVENTION LOGBOOK

The daily logbook consists of the following page replicated for each day of the study:

Thursday July 12/07

How would you describe your day today?

Good ☺ Neutral ☺ Bad ☺

Please explain why:_____

_____

_____

Please circle the number that best describes:

No pain	0 1 2 3 4 5 6 7 8 9 10	Worst possible pain
Not tired	0 1 2 3 4 5 6 7 8 9 10	Worst possible tiredness
Not nauseated	0 1 2 3 4 5 6 7 8 9 10	Worst possible nausea
Not depressed	0 1 2 3 4 5 6 7 8 9 10	Worst possible depression
Not anxious	0 1 2 3 4 5 6 7 8 9 10	Worst possible anxiety
Not drowsy	0 1 2 3 4 5 6 7 8 9 10	Worst possible drowsiness
Best appetite	0 1 2 3 4 5 6 7 8 9 10	Worst possible appetite
Best feeling of wellbeing	0 1 2 3 4 5 6 7 8 9 10	Worst possible feeling of wellbeing
No shortness of breath	0 1 2 3 4 5 6 7 8 9 10	Worst possible shortness of breath
Other problem	0 1 2 3 4 5 6 7 8 9 10	

Classification of Activities

01 - Walking
02 - Resistance Exercise Program
03 - Housework
(making meals, doing laundry, cleaning)
04 - Lawn & Garden
(picking flowers, watering lawn or garden)
05 - Lying
(resting, sleeping)
06 – Sitting
(reading or watching television)
07 - Self Care
(bathing, dressing, eating)
08 - Transportation
(riding in a car or bus, driving)
09 – Other

Rating of Perceived Exertion (RPE)

0 Nothing at all
0.5 Very, very light
1 Very light
2 Light
3 Moderate
4 Somewhat hard
5 Hard
6
7 Very hard
8
9
10 Very, very hard

Time of Day	Activity Number	Duration (minutes)	RPE (0-10)	Comments
Morning				
Afternoon				
Evening				

APPENDIX IV-4

PILOT INTERVENTION CONSENT FORM

A PILOT STUDY TO TEST THE FEASIBILITY OF A PHYSICAL ACTIVITY INTERVENTION IN ADVANCED CANCER PATIENTS

CONSENT FORM

This form is part of the process of informed consent. It is designed to explain this research study and what will happen to you if you choose to be in this study.

If you would like to know more about something mentioned in this consent form, or have any questions at anytime regarding this research study, please be sure to ask the study coordinator Sonya Lowe (902-5588). Read this consent form carefully to make sure you understand all the information it provides. You will get a copy of this consent form to keep. You do not have to take part in this study and your care does not depend on whether or not you take part.

Your participation in this study is entirely voluntary. Please take your time to make your decision. It is recommended that you discuss with your friends and/or family about whether to participate in this study.

"WHY IS THIS STUDY BEING DONE?"

You are being asked to take part in this study because you have advanced cancer. Previous studies of early stage cancer patients have shown that following a physical activity program can help increase quality of life by maintaining strength and fitness, and controlling fatigue. This is the first study to examine the effects of physical activity on patients with advanced cancer, although previous studies have shown benefits from physical activity at early stages of cancer.

This study is being done because at present, we do not know if physical activity is beneficial at your stage of cancer. It is important to test this in a study so that doctors and nurses are able to advise patients about the potential benefits and risks of physical activity at your stage of cancer.

"WHAT DO WE HOPE TO LEARN?"

We hope to learn whether advanced cancer patients are interested in taking part in a physical activity program, how well they are able to follow the program, and if there are changes in quality of life and functional abilities over the course of the program.

The purpose of this study is to test the feasibility of a physical activity program in advanced cancer patients, with the goal of gathering information to lead a larger study in the future if the results are encouraging.

"WHAT IS INVOLVED IN THIS STUDY?"

In this study, you will be prescribed a physical activity program. The program will be individually designed for you on the basis of the tests performed at the start (described below). It will last for 6 weeks and you will perform physical activity for 3 to 5 days per week. The program will comprise of walking, muscle strengthening and balance training exercises. It will take place in your home at a time that is convenient to you. You will receive initial instruction from either a study investigator or professional exercise therapist, and supervised home visits or follow-up telephone interviews three times a week with them. You will be asked to wear a pedometer throughout the study, which will count the number of steps that you take, and to record your activities in a daily logbook.

"HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?"

About 20 people will take part in this study. They will all be advanced cancer patients from the Cross Cancer Institute or Capital Health Regional Palliative Home Care.

"WHAT WILL MY PARTICIPATION INVOLVE?"

If you take part in this study, you will be prescribed an individualized physical activity program involving walking, muscle strengthening and balance training exercises that you can do in your home at a time that is convenient for you. You will receive specific instruction from either a study investigator or a professional exercise therapist as to how to perform each physical activity. You will be performing the muscle strengthening and balance training exercises 3 times a week, and you will be walking at least 2 times per week, for a total of 6 weeks. You may be doing the muscle strengthening/balance training exercises and walking on the same day or different days. You may be using ankle/wrist cuff weights and/or resistance bands for the muscle strengthening exercises, if prescribed by the professional exercise therapist. The following tests will be performed before starting the physical activity program and again at the end so that any changes can be measured:

1) Walking test: this involves walking up and down a course completing as many laps as possible in 6 minutes. This will take place in your home.

2) Functional tests: this involves performing simple activities that are part of a normal life: (30 second chair stand, 6 minute walk, chair sit-and-reach, back scratch, 8-foot up-and-go, four test balance, grip strength). Again, this test will take place in your home.
3) Questionnaire: the study investigator will do a face-to-face interview survey with you at your home that will take approximately 45 minutes. This will be repeated after you have finished the physical activity program.

During the 6 weeks, you will also be asked to wear a pedometer to keep track of the number of steps that you take. You will also be asked to record your activities in a daily logbook that will be provided to you.

"HOW LONG WILL I BE INVOLVED IN THE STUDY?"

The physical activity program will last for 6 weeks. We will contact you after the program is completed to do the final interview survey.

"WHAT ARE THE SIDE EFFECTS?"

Beginning a physical activity program can sometimes cause sore muscles and fatigue the first few times. This is normal and is generally not a threat to your health. However, if the soreness persists more than five days, or seems to be associated with an injury, you should consult a physician.

It is possible that some of the side effects of advanced cancer may be aggravated by physical activity (fatigue, pain, cardiac problems). These risks will be minimized by having your program individually designed for you according to your health and fitness level, and by instruction and guidance from either the study investigators or professional exercise therapists.

If you have any side effects, or if you want more information, you should call the project coordinator in charge of the study. The telephone number is on the last page of this form.

"WHAT ARE MY ALTERNATIVES?"

Your doctor will discuss with you other options available for enhancing quality of life and explain the benefits and risks of these. Current options involve being referred to the psychology or physiotherapy department at the Cross Cancer Institute.

You may choose not to participate in this study. This will not impact your cancer treatment or care.

"ARE THERE ANY BENEFITS TO PARTICIPATING IN THIS STUDY?"

Participation in this study may or may not be of personal benefit to you. However, based on the results of this study, it is hoped that, in the long-term, patient care can be improved.

"CAN I WITHDRAW FROM THIS STUDY?"

Taking part in this study is voluntary; you may withdraw from the study at any time if you wish to do so. Should you decide to withdraw from the study at any time, information collected on you up until that point would still be provided to the study coordinator.

"ARE THERE COSTS TO ME FOR TAKING PART IN THIS STUDY?"

There are no financial costs to you for participating in this study. All the function tests and consultations with professional exercise therapists are provided free. Ankle/wrist cuff weights and therabands will be provided for you if prescribed by the professional exercise therapists.

"WHAT ARE MY RIGHTS AS A PARTICIPANT?"

If you suffer an injury or become ill as a result of participating in this research, you will receive all medical treatments (or services) recommended by your doctors. No compensation will be provided beyond this point. However, it is important to note that nothing said in this consent form alters your legal rights to recover damages (e.g. legal action).

"WILL MY PERSONAL INFORMATION BE KEPT CONFIDENTIAL?"

Identifiable health information will be collected during this study. This information may be used by the researchers who are carrying out this study, and may be disclosed to others as described below. Any research proposal to use information that identifies you for a purpose other than this study must be approved in advance by the ACB Research Ethics Board.

Direct access to your identifiable health information collected for this study will be restricted to the researchers who are directly involved in this study except in the following circumstances:

Your identifiable health information may need to be inspected or copied from time to time for quality assurance (to make sure the information being used in the study is accurate) and for data analysis (to do statistical analysis that will not identify you). The following organizations may do this inspection:

- Alberta Cancer Board Research Ethics Board, the institutional review board at this centre
- Health Canada

Any disclosure of your identifiable health information will be in accordance with the Alberta Health Information Act. As well, any person from the organizations looking at your records on-site at the Cross Cancer Institute will follow the relevant Alberta Cancer Board policies and procedures that control these actions. Any disclosure of your identifiable health information to another individual or organization not listed here will need the approval of the Alberta Cancer Board Research Ethics Board.

Your identifiable health information collected as part of this study which includes records of your progress and your responses to the questionnaires will be kept confidential in a secure Alberta Cancer Board facility.

The researchers who are directly involved in your study may share information about you with other researchers, but you will not be identified in that shared information except by a number. The key that indicates what number you have been assigned will be kept secure by the researchers directly involved with your study and will not be released.

Although absolute confidentiality can never be guaranteed, the Alberta Cancer Board will make every effort to keep your identifiable health information confidential, and to follow the ethical and legal rules about collecting, using and disclosing this information in accordance with the Alberta Health Information Act and other regulatory requirements.

"WHO DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?"

For information about your disease and/or research related injury/illness, you may contact the Principal Investigator (Kerry Courneya, 492-1031) or study coordinator (Sonya Lowe, 902-5588) or page them through the Cross Cancer Institute Switchboard at (780) 432-8771 to answer any questions you have about this study.

If you feel, at any time, that you have not been informed to your satisfaction about the risks, benefits, or alternatives of this study, or that you have been encouraged to continue in this study after you wanted to withdraw, you can call the Patient Representative at (780) 432-8585.

UNDERSTANDING OF PARTICIPANTS

I can refuse to take part or withdraw from this study at any time without jeopardizing my health care. If I continue to take part in the study, I will be kept informed of any important new developments and information learned after the time I gave my original consent.

I also give consent for the Principal Investigator and the Alberta Cancer Board (the Custodian) to disclose identifiable health information, as per the Alberta Health Information Act, to the organizations mentioned on the previous page.

I have read and understood all of the information in this consent form. I have asked questions, and received answers concerning areas I did not understand. I have had the opportunity to take this consent form home for review and discussion. My consent has not been forced or influenced in any way. I consent to participate in this research study. Upon signing this form I will receive a signed copy of the consent.

(PRINT NAMES CLEARLY)

Name of Patient	Signature of Patient	Date &Time
Name of Witness	Signature of Witness	Date & Time
Name of Person Obtaining Consent	Signature of Person Obtaining Consent	Date & Time
Name of Investigator	Signature of Investigator	Date & Time

APPENDIX IV-5

PILOT INTERVENTION PARTICIPANT INFORMATION LETTER

HOME-BASED PHYSICAL ACTIVITY PROGRAM FOR ADVANCED CANCER

It is important for us to understand the role of physical activity during your illness. Currently we do not know how physical activity and quality of life are related in people with advanced cancer. The goal of this study is to find out whether a home-based physical activity program could be used to improve your physical function and overall quality of life.

One researcher and one exercise therapist will visit you in your home and supervise a 6-week long physical activity program in your home. The program will include two components: 1) walking, and 2) basic strength training using therabands and ankle/wrist weights. You will also be asked to wear an activity monitor which measures the amount of time that you spend walking, standing, sitting and lying down. All supervision and all equipment is provided to you free of charge for the duration of the study.

Both before and after the 6-week program, the researcher and exercise therapist will administer an interview questionnaire and basic physical function tests with you in your home. During the interview, you will be asked about your quality of life, your current symptoms, and your level of physical function. During the physical function tests, you will be asked to walk, to transfer from sitting in a chair to standing, and to try seated strength and flexibility tests.

The entire study will be carried out and supervised in your home at your convenience. The researcher and exercise therapist will provide individual supervision in your home, and will tailor the physical activity program to your level of physical functioning and ability.

CONTACT:

Sonya Lowe, Study Coordinator. (T) 902-5588

APPENDIX IV-6

PILOT INTERVENTION ETHICAL APPROVAL

Alberta Cancer Board

Provincial Office
1220 Standard Life Building
10405 Jasper Avenue
Edmonton, Alberta
Canada T5J 3N4
Tel: (780) 412-6300

ACB Provincial Office
Edmonton

Tertiary Cancer Centres
Cross Cancer Institute
Tom Baker Cancer Centre

Associate Cancer Centres
Central Alberta Cancer Centre
(Red Deer)
Grande Prairie Cancer Centre
Lethbridge Cancer Centre
Medicine Hat Cancer Centre

Community Cancer Centres
Barrhead
Bonnyville
Camrose
Canmore
Drayton Valley
Drumheller
Ft. McMurray
High River
Hinton
Lloydminster
Peace River

Division of Population Health and Information
Calgary

Medical Affairs and Community Oncology
Edmonton

Research
Edmonton

Alberta Cancer Foundation
Accepts donations in support of ACB facilities and programs.
Toll free: 1-866-412-4222

www.cancerboard.ab.ca

ALBERTA CANCER BOARD

2 April 2007

Dr. Kerry Courneya
Faculty of Physical Education
University of Alberta

Dear: Dr. Courneya:

RE: ETH-23408: A pilot study to test the feasibility of a physical activity intervention in advanced cancer patients

The Research Ethics Board (full board) met on 13 March 2007 to discuss the above protocol. Thank you for your response to my correspondence dated 19 March 2007. I am pleased to grant approval to your participation in the above noted study on behalf of the Research Ethics Board (REB). The following documents have been reviewed and approved as of 2 April 2007:

- Protocol (Version 1.0 dated 12 February 2007 including Appendices A-D)
- Consent Form (dated 27 March 2007)

Please note that this approval is based on the following conditions:

- a copy of the informed consent form must be given to each research subject and consent obtained prior to enrollment on the study;
- if there are any other changes to the protocol or consent form during the year, or if any serious adverse events to the treatment are found, a letter describing the changes/reactions must be forwarded to the REB as per the Alberta Cancer Board Policy 8.1.2 together with an updated consent form;
- an Annual Renewal form must be submitted two months prior to the deadline date of **13 March 2008** (one year from date of the convened REB meeting), containing the information as per our annual renewal form;
- a Final Report must be submitted at the termination of the project.

The deliberations of the REB included all elements described in Section 50 of the Health Information Act, and found the study to be in compliance with all the applicable requirements of the Act. The REB determined that consent will be obtained from study participants for disclosure of the health information to be used in the research.

The Alberta Cancer Board REB, complies with the following guidelines and regulations:

- Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans;

- Health Information Act which has been proclaimed on April 25, 2001 in Alberta;
- Health Canada, as defined in C.05 (Part C Division 5) (1024-Clinical Trials) of the Food And Drug Regulations-Amendment and the Therapeutic Products Directorate Guidelines/ICH Harmonized Tripartite Guidelines-Good Clinical Practice: Consolidate Guidelines;
- National Institutes of Health-Code of Federal Regulations (USA); and
- Our institution has been approved by the Office for Human Research Protections in the United States.

Members of the REB who are named as investigators or co-investigators in research studies do not participate in discussion related to, nor vote on, such studies when they are presented to the REB.

Please note that this study has been referred to as ETH-22408 in error. The correct reference number is ETH-23408.

Please accept the Board's best wishes for success in your research.

Sincerely,

Scott North, MD
Chair, Research Ethics Board

/hr

PC: Sonya Lowe
CPA
Caroline Shewchuk
OIPC

Health Research Ethics Board

2J5 Heritage Medical Research Centre
University of Alberta, Edmonton, Alberta T6G 2S2
p. 780.492.9724 (Biomedical Panel)
p. 780.492.9802 (Health Panel)
p. 780.492.0459
p. 780.492.0839
f. 780.492.2088

May 15, 2007

Dr. Kerry Courneya
Behavioral Medicine Laboratory
Faculty of Physical Education
E-488 Van Vliet Centre

Dear Dr. Courneya:

Re: A pilot study to test the feasibility of a physical activity intervention in advanced cancer patients

Thank you for submitting this application for reciprocal approval.

The Alberta Cancer Board (ACB) REB approved the above named protocol on April 2, 2007. That approval has been accepted by the University of Alberta and by its Health Research Ethics Board, and a signed document is enclosed for your records.

The ACB REB will remain your REB-of-record.

Yours sincerely,

Judith R. Abbott
Senior Coordinator
Health Research Ethics Board (Biomedical Panel)

/ja
enc.

UNIVERSITY OF ALBERTA
Capital Health Edmonton and area
CARITAS HEALTH GROUP

I. University of Alberta Institutional Authorization to Accept Alberta Cancer Board Research Ethics Board (REB)[1] Approval of an Ethics Application

II. University of Alberta Health Research Ethics Board (HREB) Acceptance of the Alberta Cancer Board REB Approval of the application titled "A pilot study to test the feasibility of a physical activity intervention in advanced cancer patients", submitted by Dr. Kerry Courneya

I. Institutional Authorization

The University of Alberta authorizes its HREB to accept the Alberta Cancer Board REB approval of the above named ethics application. This authorization is made pursuant to the *Tri-Council Policy Statement* amendment that permits "[a]n institution...[to]...authorize its REB(s) to accept the review of other REBs constituted under the Tri-Council Policy Statement."[2] Via its deemed amendment clause, the *University of Alberta Standards for the Protection of Human Research Participants* (GPC 66) permits this authorization.[3]

Vice-President (Research), University of Alberta
Dr. G. Kachanoski — Date: May 11/07

Acting Chair, University Committee on Human Research Ethics
Dr. W.A. McBlain — Date: May 7/07

II. HREB Acceptance

The University of Alberta HREB accepts the Alberta Cancer Board REB approval of the ethics application titled "A pilot study to test the feasibility of a physical activity intervention in advanced cancer patients", for Dr. Kerry Courneya

Chair, University of Alberta HREB (Biomedical Panel)
Dr. S.K.M. Kimber — Date: 2-5-2007

[1] Also referred to as the "Alberta Cancer Board *Research Ethics Committee*."

[2] Revision and amendment to Article 1.2, B1, Section 1, Ethics Review, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, stating that "Each institution is accountable for the research carried out in its own jurisdiction or under its auspices. An institution can authorize its REB(s) to accept the review of other REBs constituted under the Tri-Council Policy Statement if it so wishes."

[3] GPC66.1.1 Definitions, Purview of the *UA Standards for the Protection of Human Research Participants* [excerpted], "From time-to-time as the Ethical Principles and/or requirements of the Articles of the Tri-Council Policy [Statement] are revised or amended any such revision or amendment shall be deemed to be an amendment and revision to corresponding sections of the UA Standards."

Filing: Human Research Protections Office; Vice-President (Research); Chair, HREB (A); Chair, HREB (B); Alberta Cancer Board REB.